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1. *The Associating Effect of the Hydrogen Atom. Part VII. The N–H–N Bond. Derivatives of Pyrazole and Indazole.*

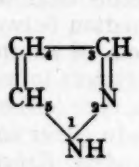
By HERBERT T. HAYES and LOUIS HUNTER.

Contrasts in boiling point, solubility in donor solvents, and degree of association are shown between derivatives of pyrazole and indazole possessing a free imino-hydrogen atom and those in which this atom has been replaced by an alkyl, aryl, or acyl group. The high values of these properties of the former class of compound are attributed to hydrogen-bond formation involving the imino-hydrogen atom. Cryoscopic measurement of molecular weight of sixteen derivatives is made over a range of concentration in benzene or in naphthalene solution. A possible mechanism of pyrazole tautomerism is proposed.

THE rarity of compounds containing the hydrogen bond connecting two nitrogen atoms is due chiefly to the comparative weakness of the N–H–N bridge. This weakness manifests itself also in the tendency shown in numerous compounds (see, *inter alia*, Part V, J., 1940, 166) in which the possibility exists of the alternative operation of various types of hydrogen bond (O–H–O, O–H–N, N–H–N), for the more stable types to assume ascendancy, and for the N–H–N bonds to contribute little, if at all, towards the structure and properties of such compounds. Again, cyclic systems which include the N–H–N bridge are more than usually sensitive to steric influences, for the bond does not survive strains which distort too greatly the normal linear distribution of the hydrogen valencies; for this reason, five-membered cyclic systems including the N–H–N bridge are extremely rare, the majority containing six, or perhaps more, members.

Almost all authentic examples of the N–H–N bridge are confined to compounds which exhibit virtual tautomerism; *i.e.*, the alternative attachment of the hydrogen atom to one nitrogen or the other can be accommodated by a suitable adjustment of valencies within the molecule. It is true that there are numerous indications of weak N–H–N bonds in systems not conforming to this condition (see, *e.g.*, the spectroscopic work of Gordy, *J. Chem. Physics*, **7**, 1939, 167; Buswell, Downing, and Rodebush, *J. Amer. Chem. Soc.*, 1939, **61**, 3252; Gordy and Stanford, *ibid.*, 1940, **62**, 497), but in these examples the bond is seldom, if ever, sufficiently stable to manifest itself in enhanced molecular weight.

In the present investigation the existence of the N–H–N bridge in derivatives of pyrazole and indazole is inferred from their physical properties, particularly their molecular weights. The virtual tautomerism of the pyrazoles follows from the researches of Knorr and v. Auwers,



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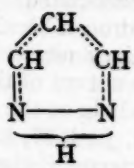

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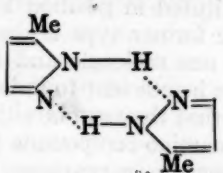

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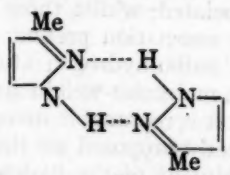


(b.)

(III.)

who demonstrated the equivalence of the 3- and the 5-position in the pyrazole nucleus (I). As a result of this there are only two mono-*C*-substituted derivatives of pyrazole.

The symmetry (see II) of the pyrazole nucleus is immediately destroyed when the imino-hydrogen atom (position 1) is substituted; there are then three different mono-*C*-substituted isomerides [*e.g.*, 1-phenyl-3 (or 4, or 5)-methylpyrazole].

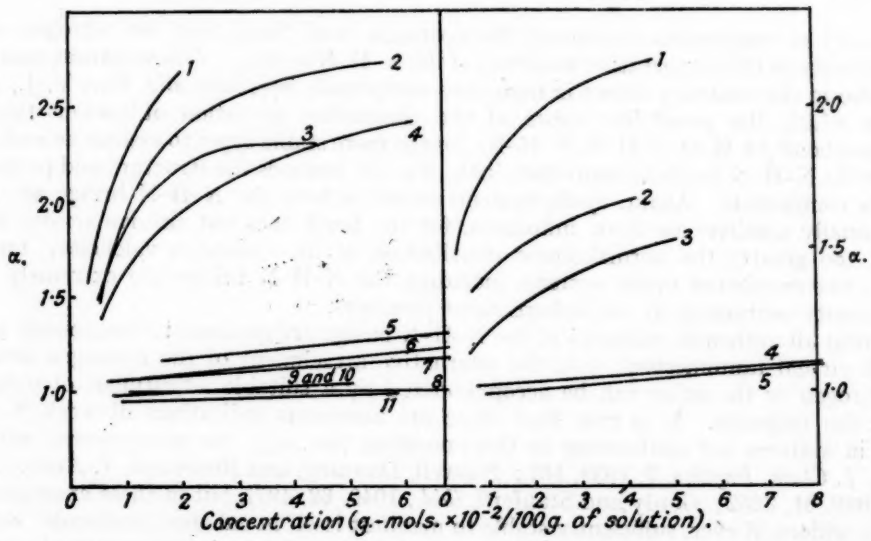
A comparison of the b. p.'s of isomeric pyrazoles (Table I) reveals the superior volatility of those isomers having substituents in the 1-position. The relatively high b. p.'s of the isomers possessing a free imino-group suggest some degree of molecular complexity in these compounds, and measurements of molecular weight of both types of pyrazole derivative over a range of concentration in benzene solution have therefore been undertaken.

TABLE I.

	B. p.		B. p.		B. p.
(Pyrazole	188°)	1 : 3 : 4-Trimethylpyrazole	160°	1-Phenyl-3-methylpyrazole	255°
1-Methylpyrazole	127	1 : 3 : 5-Trimethylpyrazole	170	1-Phenyl-4-methylpyrazole	266
3-Methylpyrazole	205	1 : 4 : 5-Trimethylpyrazole	177	1-Phenyl-5-methylpyrazole	263
4-Methylpyrazole	205	3 : 4 : 5-Trimethylpyrazole	233	3-Phenyl-1-methylpyrazole	281
		(1 : 3 : 4 : 5-Tetramethylpyrazole	193)	3-Phenyl-5-methylpyrazole	327
1 : 3-Dimethylpyrazole	136				
1 : 5-Dimethylpyrazole	153	1-Phenylpyrazole	246		
3 : 4-Dimethylpyrazole	222	3-Phenylpyrazole	313		
3 : 5-Dimethylpyrazole	218				

The results are represented in Figs. 1 and 2, which show the variation of the association factor (α) with concentration; a steep curve is interpreted as a high degree of association,

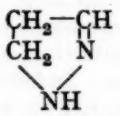
FIG. 1. FIG. 2.



and a flat or gently sloped curve as non-association. With remarkable regularity the substances measured fall into two classes, those having a free imino-hydrogen atom being associated, whilst those substituted in position 1 are unassociated. It seems clear that the association present in the former type is due to hydrogen-bond formation between the imino-hydrogen atom of one molecule and the tertiary nitrogen atom of another. The molecular-weight data are insufficient to indicate the nature of the polymers formed, but it is reasonable to assume that they can be either the chain or the cyclic type (or both) already proposed for the diazoamino-compounds (Hunter, J., 1937, 320). In either case, treatment of the hydrogen bond as a resonance phenomenon (Sidgwick, *Ann. Reports*, 1933, **30**, 112; Pauling, "The Nature of the Chemical Bond," Cornell, 1939) will provide a satisfactory explanation of the virtual tautomerism of the pyrazoles. For example, formula (III) represents two unperturbed forms of a cyclic dimer, of which the resonance hybrid may well contribute to the structure of methylpyrazole in benzene solution; the

dissociation of (III*a*) into 5- and (III*b*) into 3-methylpyrazole may then readily account for the virtual identity of these two substances. An explanation on exactly similar lines may be put forward by use of a chain polymer. The tendency of some of the curves in Fig. 1 to attain a maximum value of α in the neighbourhood of 2 may point to a preponderance of dimers in all but very dilute solutions, although there is no evidence to show that these are cyclic. This view of the tautomerism of the pyrazoles is in direct opposition to that of Pauling (*op. cit.*, p. 427).

The close parallel between association and tautomeric character is also borne out by the behaviour of pyrazoline (IV) and its derivatives. In these compounds the conjugated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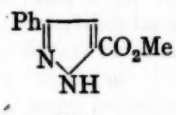
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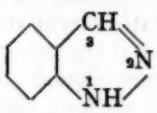

(VI.)

system is destroyed by the saturation of one double bond, thus removing the possibility of tautomerism, and it is significant that the pyrazolines possess consistently lower boiling points (Table II) than the corresponding pyrazoles. Determination of the molecular

TABLE II.

	B. p.		B. p.
Pyrazole	188°	Pyrazoline	144°
3 : 4 : 5-Trimethylpyrazole	233	3 : 5 : 5-Trimethylpyrazoline	158
3- and 4-Methylpyrazole	205	5-Methylpyrazoline	180

weights of 5-methyl- and 3 : 5 : 5-trimethyl-pyrazoline indicates that they are substantially unimolecular over a considerable range of concentration. Thus, in spite of the presence in these compounds of a free imino-hydrogen atom and a donor (tertiary) nitrogen atom, hydrogen-bond association appears to be prevented owing to the inability of the molecule to accommodate tautomeric change except by becoming a zwitterion. The case is exactly similar to that of the imino-ethers (Part I, J., 1937, 1114).

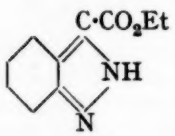
It is not surprising that the two types of pyrazole derivative show contrasts in regard to their solubility. Those which are *N*-substituted are very soluble in all organic solvents, but are insoluble in water even when hot; those possessing a free imino-group, on the contrary, are sparingly soluble in benzene and in other hydrocarbon solvents, but readily soluble in alcohol and in hot water. Similar behaviour has already been recorded for the acid hydrazides (Part VI, J., 1940, 334), the solubility in electron-donor solvents of those compounds (hydrazides and pyrazoles) possessing a free imino-group being due no doubt to hydrogen-bond formation with solvent molecules.

In a recent paper by von Auwers (*Annalen*, 1934, **508**, 51) a new aspect of pyrazole tautomerism is discussed which cannot be overlooked, for it revokes in a large measure many of the earlier conclusions. The remarkable statement is made (and accepted in other quarters; *e.g.*, Karrer, "Organic Chemistry," 1938, p. 728) that the 3- and the 5-position in the pyrazole nucleus can no longer be regarded as equivalent, and that the pyrazoles must be considered to be equilibrium mixtures of both tautomers in which the position of the equilibrium varies with the substituent groups; certain extreme cases are considered to be virtually homogeneous substances of fixed structure, *i.e.*, the imino-hydrogen atom occupies one position almost exclusively. It is to be observed that in the extreme cases quoted by von Auwers the hydrogen atom regarded as fixed is always adjacent to a substituent ester group, as in methyl 3-phenylpyrazole-5-carboxylate (V), and it appeared to us that the fixation might be a result of chelate ring formation through the imino-hydrogen atom and the carbonyl oxygen. If this were the case, it should be reflected in a much reduced degree of association. Experiment shows, however, that far from being unassociated, such esters are even more highly associated (Fig. 1, curve 1) than are pyrazoles which lack the ester group, and the increased association must clearly be due to N–H–O bonds, rendered possible by the introduction of the ester group. The

construction of models reveals no stereochemical objection to the existence of polymers containing the N–H–O bridge, and involving either one nitrogen atom or the other. Molecular-weight evidence, therefore, provides no confirmation of von Auwers's conclusions, although the isolation of chelate metallic derivatives (IX) (see below) accords them some measure of support. The behaviour of the pyrazole-5-carboxylic esters recalls the recent observation by Pratesi and Berti (*Atti X Congr. Internaz. Chim.*, 1938, III, 313) that the pyrrole-α-aldehydes are associated (dimeric) in benzene solution, and that both their molecular association and their tautomeric (aldehyde–hydroxymethine) character are destroyed by replacement of the imino-hydrogen atom.

Measurements of molecular weight have also been performed on indazole (VI) and a few of its derivatives;* the inferior solubility of the associated compounds of this series necessitated the use of naphthalene as a cryoscopic solvent. The results (Fig. 2) lead to conclusions similar to those reached for their pyrazole analogues. Indazole itself (curve 3) shows a high degree of association even in naphthalene solution, in which the high temperature (80°) of the cryoscopic determination would be expected to reduce the association owing to thermal agitation. 1-Methyl- and 1-acetyl-indazole (curves 4 and 5), on the other hand, are unassociated at the much lower temperature (5°) of melting benzene. Solubility contrasts similar to those in the pyrazole series are also apparent; indazole itself can even be recrystallised from hot water.

Attempts have been made to fix the imino-hydrogen atom of the indazole nucleus on the 2-nitrogen atom by substituting suitable electron-donor groups in position 3. Such fixation is not confirmed, however, in the values of α obtained (Fig. 2, curve 1) for ethyl indazole-3-carboxylate (VII), which, like its pyrazole analogue (V), is more highly



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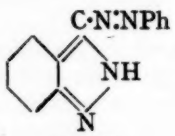

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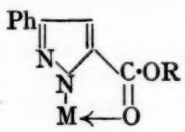

(IX.)

associated than the parent indazole. Similarly, 3-benzeneazoindazole (VIII) shows a higher degree of association (Fig. 2, curve 2) than that of indazole, and it is clear that the high association of both (VII) and (VIII) is the result of the simultaneous operation of homogeneous and heterogeneous hydrogen-bond association (see Part V, *loc. cit.*).

The absence of chelation in pyrazole and indazole derivatives possessing donor substituents on the carbon atom adjacent to nitrogen [as in (V), (VII), and (VIII)] is probably due to steric factors connected with the strain of five-membered ring systems involving the hydrogen bond. Fixation of structure can be achieved, however, by replacing the imino-hydrogen atom by certain metallic atoms, for which the much reduced valency angle (compared with that of hydrogen) can bring about considerable relief of strain in a five-membered system. For instance, a series of metallic (copper, nickel, cobalt) derivatives of (V), (VII), and (VIII) has been prepared, the properties of which leave no doubt of their chelate nature; they must therefore contain a five-membered chelate ring as in (IX; M = 1 equiv. of metal), which represents the metallic compound derived from (V). These chelate metallic derivatives, the preparation and properties of which will be described elsewhere, are evidently derived from parent imino-compounds of the fixed structure denoted in (V), (VII), and (VIII).

In the following tables concentrations are expressed as g.-mols. $\times 10^{-2}$/100 g. of solution, the formula weights appearing in parentheses; *M* is the apparent molecular weight deduced according to the ideal-solution laws; and the association factor (α) is calculated as the ratio of *M* to the formula weight. The cryoscopic solvent is benzene except where otherwise stated. Conclusions as to molecular association are based, not on the absolute

* The old distinction between indazole and *iso*indazole is now invalid, the imino-hydrogen atom not being definitely located on either nitrogen atom; but two isomeric *N*-substituted indazoles are distinguishable, according as the substituent is attached at position 1 or 2 (see VI).

values of α, which may have no quantitative significance, but rather on the slope of the association–concentration curves. By comparing the slopes of these curves for substances of similar constitution, errors arising from departures from the ideal laws are very much diminished.

Fig. 1.

	Concn.	*M.*	α.
Ethyl 3-phenylpyrazole-5-carboxylate (216) (Curve 1)	0·33	341	1·58
	0·65	425	1·965
	1·28	522	2·42
	1·89	578	2·68
5-Phenyl-3-methylpyrazole (158) (Curve 2)	0·495	233	1·47
	1·575	371	2·35
	2·72	400	2·53
	4·00	419	2·65
	5·59	434	2·74
5-Ethoxy-3-methylpyrazole (126) (Curve 4)	0·545	176	1·39
	1·61	231	1·83
	2·63	257	2·04
	4·13	284	2·25
	6·06	305	2·42
3 : 5 : 5-Trimethylpyrazoline (112) (Curve 5)	1·685	131	1·17
	3·82	136	1·21
	5·67	142	1·27
	7·51	147	1·31
	9·27	153	1·36
5-Ethoxy-1-phenyl-3-methylpyrazole (202) (Curve 9)	0·72	198	0·98
	1·88	201	0·99
	2·87	200	0·99
	3·84	204	1·01
	5·05	207	1·02
5-Benzoyloxy-1-phenyl-3-methylpyrazole (278) (Curve 10)	0·53	266	0·96
	1·05	265	0·95
	1·80	268	0·96
	2·74	272	0·98
	3·85	276	0·99
	5·09	281	1·01
3 : 5-Dimethylpyrazole (96) (Curve 3)	0·47	143	1·485
	1·83	206	2·145
	3·145	221	2·30
	4·42	221	2·30
5-Methylpyrazoline (84) (Curve 6)	1·61	90	1·07
	3·62	94	1·12
	5·65	100	1·19
	7·65	104	1·23
	10·40	110	1·31
1 : 3 : 5-Trimethylpyrazole (110) (Curve 7)	0·76	115	1·04
	2·22	120	1·09
	4·22	122	1·11
	6·12	125	1·14
	8·23	126	1·15
1-Phenyl-3 : 5-dimethylpyrazole (172) (Curve 8)	1·05	173	1·01
	2·49	171	1·00
	4·22	170	0·99
	6·00	171	1·00
	7·74	174	1·01
1 : 5-Diphenyl-3-methylpyrazole (234) (Curve 11)	0·91	225	0·96
	2·38	228	0·97
	3·41	227	0·97
	4·62	228	0·975
	5·94	231	0·99

Fig. 2.

	Concn.	*M.*	α.
Ethyl indazole-3-carboxylate (190) (*in naphthalene*) (Curve 1)	0·35	281	1·48
	0·70	317	1·67
	1·37	343	1·80
	2·35	382	2·01
	3·29	398	2·09
	4·49	409	2·15
Indazole (118) (*in naphthalene*) (Curve 3)	0·55	137	1·16
	1·09	139	1·18
	1·63	153	1·30
	2·41	158	1·33
	3·45	167	1·42
	4·94	180	1·52
3-Benzeneazoindazole (222) (*in naphthalene*) (Curve 2)	0·59	300	1·35
	1·16	319	1·44
	1·715	328	1·48
	2·53	351	1·58
	3·31	362	1·63
	4·06	372	1·67
1-Methylindazole (132) (Curve 4)	0·81	133	1·01
	2·13	137	1·03
	4·10	137	1·03
	6·38	140	1·06
	9·16	147	1·11
1-Acetylindazole (160) (Curve 5)	0·93	157	0·98
	2·70	161	1·01
	4·37	166	1·085
	6·34	170	1·065
	8·17	174	1·09

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2. *A Determination of Molecular Symmetry in the αβ-Diethyldibenzyl Series.*

By C. H. Carlisle and Dorothy Crowfoot.

X-Ray crystallographic measurements on a number of compounds belonging to the diethylstilbene and diethyldibenzyl series have been carried out. These have proved that the higher-melting isomers in the diethyldibenzyl series which are derived from solid diethyldibenzyl are *meso*-compounds, whereas the lower-melting isomers from liquid diethyldibenzyl are racemic.

During the preparation of diethyldibenzyl derivatives related to diethylstilboestrol, two isomeric sets of compounds are encountered which should theoretically belong severally to the *meso*- and the racemic stereoisomeric series (Dodds, Goldberg, Lawson, and Robinson, *Proc. Roy. Soc.*, 1939, *B*, **127**, 140; Kerschbaum, Kleedorfer, Prillinger, Wessely, and Zajic, *Naturwiss.*, 1939, **27**, 131). The distinction between the two series is of interest in view of the very different biological activity of the different isomers; and this distinction can be made through comparatively simple *X*-ray crystallographic measurements on certain of the compounds concerned.

The use of *X*-ray measurements in this connection depends on the fact that the individual molecules of a *meso*-compound must themselves possess symmetry, whereas those in a racemic compound or mixture are asymmetric. Detailed *X*-ray analysis necessarily reveals the molecular symmetry in the course of the complete structure determination; but this is a long process and it is often possible (cf. Astbury and Yardley, *Phil. Trans.*, 1924, *A*, **224**, 221; Bernal, *Ann. Reports*, 1933, **30**, 411) to make use of the first and rapid stages of *X*-ray measurement to deduce this property. In certain crystal structures where the molecules possess symmetry, this symmetry contributes to that of the crystal as a whole, and consequently the number of molecules in the unit cell is smaller than the number of asymmetric units required by the crystallographic space-group present. Here, simple measurement of the crystal unit cell size, density, and space-group suffices to determine the molecular symmetry. The principal limitations to the general application of these measurements are two-fold. First, often the molecular symmetry (particularly where this is high) does not appear in the crystal symmetry; and secondly, crystals occasionally show higher symmetry than that actually contributed by the molecules owing to statistical disorder in the crystal structure. In the present problem it is possible to surmount these difficulties by examining a sufficient number of different types of compounds belonging to the two series. Several of these prove favourable for the symmetry determination, and since these include a variety of chemical derivatives, the probability that statistical disorder is present and might affect the conclusions reached is extremely small.

The following table records the *X*-ray measurements carried out on the two series of diethyldibenzyl derivatives and also includes for comparison data on diethylstilboestrol and several related compounds. In the diethylstilbene series there is a double bond at the centre of the molecule, and doubtless the general arrangement of the groups around this bond is *trans*- in the compounds examined, *i.e.*, the molecules in all cases have a centre of symmetry. However, this point is clearly established by the present measurements only in the case of diethylstilboestrol dipropionate. In the other compounds the situation may be similar to that in stilbene itself, where detailed analysis has demonstrated molecular symmetry not apparent from the preliminary measurements (Robertson, *Proc. Roy. Soc.*, 1936, *A*, **154**, 187; 1937, *A*, **162**, 568). Dihydroxydiphenylhexadiene, which is different in type but may be included here, is proved by the measurements to have a centre of symmetry, as would be expected.

Seven compounds have been examined in the diethyldibenzyl series. Diethyldibenzyl itself has only been studied in the one isomeric form, the other being liquid. Of the remaining six compounds, three are derived from the solid dibenzyl (a), and three from the liquid dibenzyl (b). The *X*-ray measurements prove that solid diethyldibenzyl and

Compound.	M. p.	Space-group.	No. of asymmetric units required in unit cell.	No. of molecules in unit cell.	*a*, A.	*b*, A.	*c*, A.	*β*.	*d*.
β-Diethylstilbene	70—71°	$P2_1/c$	4	4	7·66	20·18	9·33	93°	1·071
αβ-Diethylstilboestrol + C_6H_6	171	$P2_1/a$	4	4	10·93	12·78	13·75	90	1·189
4 : 4′-Dimethoxy-αβ-diethylstilbene	123—124	$P2_1/n$	4	4	7·79	24·24	10·62	122	1·154
αβ-Diethylstilboestrol dipropionate	104	*Pbca*	8	4	9·74	8·15	27·5	—	1·142
4 : 4′-Dihydroxy-γδ-diphenyl-$\Delta^{\beta\beta}$-hexadiene	227—228	*Pcab*	8	4	18·9	5·41	14·4	—	1·184
αβ-Diethyldibenzyl (*a*)	89—90	$P2_1/a$	4	2	7·38	19·27	5·75	117	1·089
4 : 4′-Dihydroxy-αβ-diethyldibenzyl (*a*)	184	$P2/a$ approx. to Pc/a	4	4	13·93	5·96	24·39	89° 20′	(1·063)
4 : 4′-Dihydroxy-αβ-diethyldibenzyl (*b*)	128	$P2_1/n$	4	4	7·76	18·13	11·33	92	1·143
4 : 4′-Diamino-αβ-diethyldibenzyl (*a*)	140	$P2_1/a$	4	2	5·50	15·21	9·35	98	1·135
* 4 : 4′-Diamino-αβ-diethyldibenzyl (*b*)	97—98	*Cc*	4	4	10·15	19·89	7·67	89	1·136
4 : 4′-Dicarbomethoxy-αβ-diethyldibenzyl (*a*)	145—146	$P\bar{1}$	2	1	7·97	8·39	8·30	$\alpha \simeq 102$ $\beta \simeq 98$ $\gamma \simeq 113$	1·194
4 : 4′-Dicarbomethoxy-αβ-diethyldibenzyl (*b*)	95	$P2_1/a$	4	4	15·06	7·76	17·7	108	1·175

* This was the only compound of those in this table in which the test for polarity was positive.

the diamino-compound derived from it have molecules containing a centre of symmetry, since both crystallise with two molecules in the unit cell and space-groups requiring four asymmetric units. These therefore belong to the *meso*-series. The ester (a) is in a similar category except that the space-group determination, since it depends on a negative test, *viz.*, the absence of a pyroelectric effect, is not so rigid. The crystallography of the dihydroxy-derivative (a) does not provide conclusive evidence of molecular symmetry, though even here certain confirmation that this is the *meso*-form is given by the pseudosymmetry of the crystal. The remaining three compounds, derived from liquid diethyldibenzyl, all show crystal structures in which the asymmetric unit may well be the molecule itself. The positive pyroelectric effect shown by diaminodiethyldibenzyl (b) is perhaps some positive evidence that the molecules in this crystal have no centre of symmetry, and consequently that the crystal is racemic.

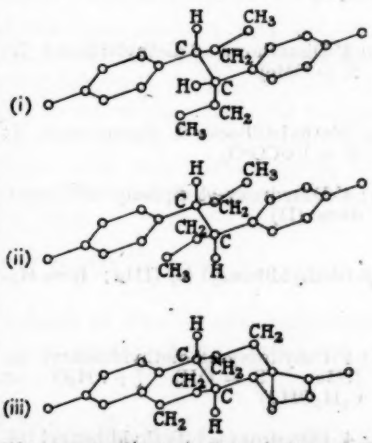


Diagram to illustrate the relation of the stereochemical form of the isomers of 4 : 4′-dihydroxy-αβ-diethyldibenzyl to that probably present in oestrone. Possible atomic arrangement in :

(i) d- *or* l-4 : 4′-*Dihydroxy-αβ-diethyldibenzyl* (*series b*).
(ii) meso-4 : 4′-*Dihydroxy-αβ-diethyldibenzyl* (*series a*).
(iii) *Oestrone.*

There are similarities, though not very close, between the crystallography of certain members of both isomeric series and that of oestrone or other compounds of the natural sex-hormone and sterol series. These similarities probably express little more than the fact that the configurations of the molecules of both diethyldibenzyl series are of an extended form, perhaps that illustrated in the figure, or the variety found in dibenzyl itself (Robertson, *Proc. Roy. Soc.*, 1935, *A*, **150**, 348). This being so, it is an interesting fact that the stereochemical arrangement of the atoms in the *meso*-series of diethyl derivatives (a) above, which is biologically the most active series, is very closely related to the stereochemical form deduced for the natural sex hormones. The fact that the *meso*-compounds have a centre of symmetry in the crystals proves that the disposition of the atoms about the central carbon–carbon bond is of the *trans*-type considered

characteristic of the junction between rings B and C of the sterol sex-hormone series (see figure).

Experimental.

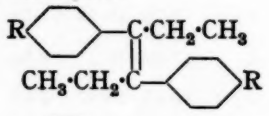
X-Ray Technique.—*X*-Ray single-crystal photographs of each compound, about three crystallographic axes, were taken on the Stubbins rotation-camera. In two cases, those of diethyldibenzyl and diaminodiethyldibenzyl (b), Weissenberg photographs were taken about the symmetry axes, to confirm the presence of glide elements in the respective space-groups. The cell dimensions recorded are probably correct to $\pm 1\%$.

Density.—In all cases the density was determined by the flotation method in sodium chloride solution. The probable limits of error are $\pm 0{\cdot}5\%$.

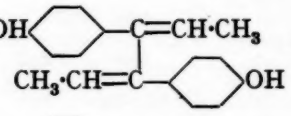
Test for Polarity.—The crystals, in turn, were placed on a well-cleaned copper plate and immersed in liquid air. A positive effect is observed if the crystals stick to the plate (Martin, *Min. Mag.*, **1931**, **22**, 519).

Morphology and Optics.

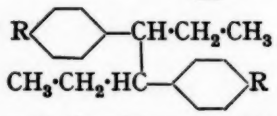
(I.)



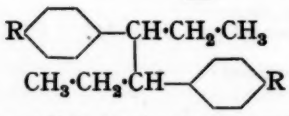
(II.)



(III*a*.)



(III*b*.)



$\alpha\beta$-Diethylstilbene (I; R = H)	Monoclinic plates, {010} dominating, bounded by {100}, {001}, and {101}. γ parallel to b, a 12° from the a axis in the acute angle. Positive. $2E \simeq 60°$.
$\alpha\beta$-Diethylstilboestrol (I; R = OH) + C_6H_6	Monoclinic prisms, elongated along [100], bounded by {010} and {001}. a parallel to b; β and γ approximately parallel to a and c respectively. Positive.
4 : 4′-Dimethoxy-$\alpha\beta$-diethylstilbene (I; R = OMe)	Monoclinic plates with {010} dominating, bounded by {100} and {001}. γ parallel to b, β 20° from the a axis in the obtuse angle. Positive. $2E \simeq 27°$.
$\alpha\beta$-Diethylstilboestrol dipropionate (I; R = Et·CO·O)	Rhombic plates, {001} dominating, bounded by {110}. a, β, and γ parallel to a, b, and c respectively. Positive. $2E \simeq 52°$.
4 : 4′-Dihydroxy-$\gamma\delta$-diphenyl-$\Delta^{\beta\delta}$-hexadiene (II)	Rhombic laths elongated along [010], bounded by {100}, {001}, and {101}. a, β, and γ parallel to b, a, and c respectively. Negative. $2V \simeq 20°$.
$\alpha\beta$-Diethyldibenzyl (a) (III*a*; R = H)	Monoclinic plates, {010} dominating, bounded by {100} and {001}. γ parallel to b; a lies 10° from the a axis in the acute angle. Negative. $2V \simeq 30°$.
4 : 4′-Dihydroxy-$\alpha\beta$-diethyldibenzyl (a) (III*a*; R = OH) [+ xH$_2$O or C_2H_5OH ?]	Monoclinic laths elongated along [010], bounded by {001} and {100}. Twins on {001}. β parallel to b, a and γ approximately parallel to a and c respectively. Positive. $2V \simeq 60°$.
4 : 4′-Dihydroxy-$\alpha\beta$-diethyldibenzyl (b) (III*b*; R = OH)	Monoclinic prisms, elongated along [100], bounded by {011} and {101}. β parallel to b, γ lies 22° from the c axis. Positive. $2V \simeq 54°$.
4 : 4′-Diamino-$\alpha\beta$-diethyldibenzyl (a) (III*a*; R = NH_2)	Monoclinic plates with {001} dominating, bounded by {010}, {110}, {011}. a parallel to b, γ lies 12° from the c axis in the acute angle. Positive. $2E \simeq 34°$.
4 : 4′-Diamino-$\alpha\beta$-diethyldibenzyl (b) (III*b*; R = NH_2)	Monoclinic plates with {001} dominating. β parallel to b, a about 17° from the a axis. Negative. $2V \simeq 60°$.
4 : 4′-Dicarbomethoxy-$\alpha\beta$-diethyldibenzyl (a) (III*a*; R = CO_2Me)	Anorthic plates with {001} dominating, bounded by {100} {010}, and {$\bar{1}$10}. Optic axial plane 25° from ⊥ to {001}. "Fast" extinction in (001) 10° to a axis in the acute angle. Negative. $2V \simeq 60°$.
4 : 4′-Dicarbomethoxy-$\alpha\beta$-diethyldibenzyl (b) (III*b*; R = CO_2Me)	Monoclinic laths elongated along [010], with faces {001}, {201}, and {010}. β parallel to b; γ lies 9° from the c axis in the acute angle. Negative. $2E \simeq 52°$.

We are indebted for material to Prof. Dodds, Dr. A. L. Bacharach, and Dr. Lester Smith, and particularly to Sir Robert Robinson and Dr. G. K. Hughes who suggested this application of our measurements.

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DEPARTMENT OF MINERALOGY and CRYSTALLOGRAPHY,
OXFORD.

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3. *The Condensation of Halogeno-pyridines, -quinolines, and -isoquinolines with Sulphanilamide.*

By MONTAGUE A. PHILLIPS.

When halogeno-pyridines, -quinolines, and *-iso*quinolines are condensed with *p*-aminobenzenesulphonamide in the presence of potassium carbonate and copper, condensation generally occurs at the sulphonamide end of the molecule, owing probably to the intermediate formation of the potassium salt of the amide. In the absence of alkali-metal carbonate, condensation occurs exclusively at the amino-end of the sulphonamide molecule in all the cases investigated. 2-Chloro-5-nitropyridine, however, in the presence of potassium carbonate and copper gives a mixture of *5-nitro*-2-(p-*aminobenzenesulphonamido*)*pyridine* and p-(5′-*nitro*-2′-*pyridylamino*)*benzenesulphonamide*, the former predominating. This is probably due to the exceedingly great reactivity of the chlorine atom in this particular pyridine derivative.

BOBRANSKI (*Arch. Pharm.*, 1939, **277**, 75) has shown that condensation of 2- and 4-chloroquinoline with sulphanilamide gives *p*-(2′- and 4′-quinolylamino)benzenesulphonamide respectively. Gray (J., 1939, 1202) has obtained *p*-(2′-pyridylamino)benzenesulphonamide by condensation of 2-chloropyridine and sulphanilamide. In connection with the scheme of chemotherapeutic study proceeding in these laboratories it has now been shown that when 2-halogeno-pyridines and -quinolines are condensed with sulphanilamide in the presence of potassium carbonate and a trace of copper powder, condensation generally occurs at the sulphonamide end of the second component, thus:

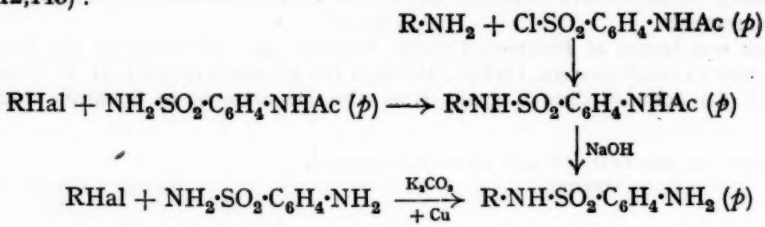
$$NH_2{\cdot}C_6H_4{\cdot}SO_2{\cdot}NH_2 + HalR \longrightarrow NH_2{\cdot}C_6H_4{\cdot}SO_2{\cdot}NHR$$

However, by fusion of the two components in the absence of alkali-metal carbonate, condensation occurs, as shown by Bobranski (*loc. cit.*), exclusively at the amino-end of the sulphonamide molecule in all the cases investigated.

$$NH_2{\cdot}SO_2{\cdot}C_6H_4{\cdot}NH_2 + HalR \longrightarrow NH_2{\cdot}SO_2{\cdot}C_6H_4{\cdot}NHR$$

Thus, 2-bromo- and 2-iodo-pyridine with sulphanilamide give *p*-(2′-pyridylamino)benzenesulphonamide and 2-(*p*-aminobenzenesulphonamido)pyridine by the Bobranski and the Ullmann method respectively, and from 2-bromoquinoline are obtained (2′-quinolylamino)-benzenesulphonamide and 2-(p-*aminobenzenesulphonamido*)*quinoline* by these two methods. 1-Chloro*iso*quinoline, when fused with *p*-aminobenzenesulphonamide, gives exclusively p-(1′-iso*quinolylamino*)*benzenesulphonamide*, which was identified by the absence of a free amino-group and by synthesis of the isomeric 1-(p-*aminobenzenesulphonamido*)iso*quinoline*, from *p*-acetamidobenzenesulphonyl chloride and 1-amino*iso*quinoline, followed by hydrolysis of the resulting 1-(p-*acetamidobenzenesulphonamido*)iso*quinoline*. The products of condensation of the 2-halogenopyridines and of 2-bromoquinoline with *p*-aminobenzenesulphonamide by the Ullmann method were also identified by this method of synthesis and also by condensation of the halogeno-pyridine or -quinoline with *p*-acetamidobenzene-

sulphonamide, followed by alkaline hydrolysis of the intermediate acetyl derivatives (see E.P. 512,145):



To account for these results it is suggested that use of potassium carbonate causes the formation of the potassium salt of the sulphonamide, which then condenses with the halogen derivative. In the absence of alkali-metal carbonate, the amino-group appears to be more reactive than the sulphonamido-group and condensation in consequence proceeds at the basic end of the sulphonamide molecule.

In accordance with this hypothesis, 2-chloro-5-nitropyridine gave by the Bobranski method exclusively p-(5′-*nitro*-2′-*pyridylamino*)*benzenesulphonamide*. When the condensation was done under the Ullmann conditions, a mixture of this compound with the isomeric 5-*nitro*-2-(p-*aminobenzenesulphonamido*)*pyridine* was obtained in which the latter predominated. No difficulty was experienced in isolating the latter compound in a practically pure condition, but its isomeride was only identified after considerable trouble. Both isomerides were subsequently identified by synthesis.

Reduction of 5-nitro-2-(*p*-aminobenzenesulphonamido)pyridine obtained by either method gave the corresponding *amino*-compound; similarly p-(5′-*amino*-2′-*pyridylamino*)-*benzenesulphonamide* was obtained from the isomeric compound made by either of the above alternative methods. Just as 2-(*p*-aminobenzenesulphonamido)pyridine is obtained from 2-bromopyridine and *p*-aminobenzenesulphonamide by the Ullmann method, so p-(2′-*pyridylamino*)*benzenesulphon*-2′-*pyridylamide* is obtained from *p*-(2′-pyridylamino)-benzenesulphonamide and 2-bromopyridine. This compound could not be obtained by the Bobranski method from 2-(*p*-aminobenzenesulphonamido)pyridine and 2-halogeno-pyridines. Attempts to obtain it from *p*-halogenobenzenesulphon-2′-pyridylamide and 2-aminopyridine also failed, presumably on account of the low order of reactivity of the halogen atom. This failure is paralleled by the failure to obtain *p*-(2′-pyridylamino)-benzenesulphonamide from *p*-bromobenzenesulphonamide and 2-aminopyridine; here also the bromine atom is relatively non-reactive.

Experimental.

2-(p-*Aminobenzenesulphonamido*)*pyridine*.—(1) A mixture of 2-bromopyridine (Craig, *J. Amer. Chem. Soc.*, 1934, **56**, 231) (4·0 g.), *p*-aminobenzenesulphonamide (4·3 g.), anhydrous potassium carbonate (3·6 g.), and copper powder (0·05 g.) was refluxed at 180° for 3 hours. The melt was dissolved in water (40 c.c.), filtered from copper, and extracted with chloroform in order to remove unchanged bromopyridine (0·9 g.). Addition of dilute acetic acid gave 2-(*p*-aminobenzenesulphonamido)pyridine, m. p. 190—191° after repeated crystallisation from 50% acetic acid.

(2) 2-Iodopyridine (Wibaut and La Bastide, *Rec. Trav. chim.*, 1933, **52**, 493) (5·2 g.) was substituted for the 2-bromopyridine in (1), and the mixture refluxed for 1 hour at 150°. The subsequent treatment gave the pyridylamide, m. p. 190—191° after recrystallisation from 50% acetic acid or aqueous acetone. Prolonged drying at 100° of the product from acetic acid is necessary in order to decompose the acetate of the base which is partially formed during crystallisation from this solvent.

(3) A mixture of 2-bromopyridine (7·9 g.), *p*-acetamidobenzenesulphonamide (10·7 g.), potassium carbonate (6·5 g.), and copper powder (0·5 g.) was refluxed for 1 hour at 220°. The mixture was dissolved in hot water (200 c.c.), filtered from copper, and acidified with dilute acetic acid, giving 2-(*p*-acetamidobenzenesulphonamido)pyridine, m. p. 224° after crystallisation from 50% acetic acid (Found: N, 14·5. Calc. for $C_{13}H_{13}O_3N_3S$: N, 14·4%). Hydrolysis by boiling with 10 parts of 2N-sodium hydroxide for 1 hour gave a 90% yield of the amino-

compound, m. p. 190° when crystallised as above. 2-Chloropyridine could not be substituted for the corresponding bromo-derivative in the above experiment.

(4) To 2-aminopyridine (9·4 g.), dissolved in dry pyridine (20 c.c.) at room temperature, was added *p*-acetamidobenzenesulphonyl chloride (24·0 g.). The temperature rose to 70°; after cooling, the mixture was treated with water, and the precipitated 2-(*p*-acetamidobenzenesulphonamido)pyridine crystallised from 50% acetic acid; m. p. 224° (Found: N, 14·4%). Its hydrolysis as in (3) gave a 90% yield of 2-(*p*-aminobenzenesulphonamido)pyridine in colourless plates or prisms, m. p. 190° (Found: C, 53·3; H, 4·5; N, 16·8; S, 12·9. Calc. for $C_{11}H_{11}O_2N_3S$: C, 53·2; H, 4·55; N, 16·8; S, 12·85%), readily soluble in dilute sodium hydroxide solution (1 mol.). From concentrated aqueous solutions alcohol precipitated the *sodium* salt in colourless plates, readily soluble in cold and slightly hydrolysed by boiling water. Aqueous solutions of the sodium salt are alkaline to phenolphthalein (Found: Na, 8·4. $C_{11}H_{10}O_2N_3SNa$ requires Na, 8·5%). The pyridylamide is soluble about 1 part in 1,000 in cold water. It is readily soluble in 2N-hydrochloric acid. The diazo-solution has a deep yellow colour; concentrated diazo-solutions deposit the diazo-compound in yellow needles, which couple normally with the usual reagents.

Action of Mineral Acids on 2-(p-*Aminobenzenesulphonamido*)*pyridine.*—The base (49·8 g.) was refluxed with 2N-hydrochloric acid for 1½ hours. On cooling, sulphanilic acid separated (34·6 g.; 75% of the calculated amount). The filtrate from this, on basification with excess of 50% sodium hydroxide solution and extraction with chloroform, gave 2-aminopyridine, m. p. 58° after washing with light petroleum, the slightly basic odour of which was devoid of the sharp smell characteristic of the distilled product obtained by amination of pyridine (Tschitschibabin and Seide, *J. Russ. Phys. Chem. Soc.*, 1915, **46**, 1216). Quantitative experiments on the acid fission of the above sulphonamide showed that about 80% was decomposed after 15 minutes' boiling with 2N-hydrochloric acid and 90% in about 30 minutes.

p-(2′-*Pyridylamino*)*benzenesulphonamide.*—A mixture of 2-bromopyridine (4·0 g.) and sulphanilamide (4·3 g.; 1 equiv.) was heated at 175° for 45 minutes. The product was dissolved in 2N-sodium hydroxide and reprecipitated, after filtration, with 2N-acetic acid. The base, crystallised from aqueous acetone, had m. p. 223—224° (Gray, *loc. cit.*, gives m. p. 235°). It was soluble in dilute sodium hydroxide solution and in dilute mineral acids, and was shown by diazo-coupling tests to be free from amino-group even in the crude material (Found: N, 16·8; S, 12·9. Calc. for $C_{11}H_{11}O_2N_3S$: N, 16·8; S, 12·85%). The same yield was obtained when 2 equivs. of either component were used in the condensation, but the time of reaction was considerably lessened.

2-(p-*Aminobenzenesulphonamido*)*quinoline.*—(1) 2-Bromoquinoline (5·2 g.), sulphanilamide (4·3 g.), potassium carbonate (3·5 g.), and copper powder (0·05 g.) were refluxed at 180° for 1½ hours. The product was dissolved in boiling water (40 c.c.) containing 5 c.c. of 2N-sodium hydroxide and, after filtration from copper, acidified with dilute acetic acid. The gum which formed slowly hardened and was boiled with 2N-sodium hydroxide (80 c.c.) for some minutes. On cooling, the sodium salt separated; this was collected and dissolved in boiling water (40 c.c.); treatment with 50% acetic acid gave a crystalline solid (3·0 g.), m. p. 194° (Found: N, 14·0. $C_{15}H_{13}O_2N_3S$ requires N, 14·05%). Diazo-tests showed the presence of a free amino-group.

(2) A mixture of 2-chloroquinoline (8·2 g.), *p*-acetamidobenzenesulphonamide (10·7 g.), potassium carbonate (6·5 g.), and copper powder (0·5 g.) was heated at 250° for 3½ hours. The product was dissolved in boiling water (100 c.c.) and filtered. Acidification of the hot filtrate (from which a potassium salt separated on cooling) with dilute acetic acid gave 5·5 g. of a solid, presumably the acetyl derivative of the above base, which was refluxed with 55 c.c. of 2N-sodium hydroxide for 1 hour. On cooling, the sodium salt of 2-(p-*aminobenzenesulphonamido*)-*quinoline* separated. This was collected and treated as in (1), giving the base (4·0 g.), m. p. 195° (Found: N, 14·1%).

(3) Coal-tar quinoline was aminated by sodamide in xylene (Tschitschibabin and Seide, *loc. cit.*; Tschitschibabin, Witkowsky, and Lapschin, *Ber.*, 1925, **58**, 805) and from the mixture of aminoquinolines and 1-amino*iso*quinoline so obtained, 2-aminoquinoline, m. p. 129°, was isolated by the method of Morgan and Stewart (J., 1938, 1302). To a solution of 2-aminoquinoline (2·0 g.) in pyridine (4 c.c.) was added *p*-acetamidobenzenesulphonyl chloride (3·2 g.). The temperature rose to 50°; after standing and dilution with water (60 c.c.) the precipitated 2-(p-*acetamidobenzenesulphonamido*)*quinoline* (3·3 g.) was crystallised from 50% acetic acid; m. p. 216° (Found for material dried at 100°: C, 59·6; H, 4·4; N, 12·3. $C_{17}H_{13}O_3N_3S$ requires C, 59·6; H, 4·5; N, 12·2%). Its hydrolysis as in (2) gave 2-(*p*-aminobenzenesulphonamido)-

quinoline, m. p. 195° (Found: C, 60·5; H, 4·4; N, 14·0; S, 10·6. $C_{15}H_{13}O_2N_3S$ requires C, 60·2; H, 4·4; N, 14·05; S, 10·7%).

2-(*p*-Aminobenzenesulphonamido)quinoline obtained by any of the above methods forms colourless plates giving a sparingly soluble, crystalline sodium salt with dilute caustic soda; with 2N-hydrochloric acid in excess it forms an insoluble hydrochloride. It is sparingly soluble in ordinary organic solvents. The diazo-solution is yellow and couples normally.

p-(2′-*Quinolylamino*)*benzenesulphonamide*.—A mixture of 2-bromoquinoline (4·2 g.) and sulphanilamide (3·4 g.; 1 equiv.) was heated at 170°. After melting, the mixture resolidified within 5 minutes; after 10 minutes' heating, the mixture was boiled with 15% hydrochloric acid (80 c.c.) for 10 minutes, and the suspension of the hydrochloride treated with excess of saturated sodium acetate solution. The base obtained (4·2 g.) was dissolved in a mixture of boiling alcohol (100 c.c.) with the requisite amount of 2N-sodium hydroxide, and the hot filtered solution treated with boiling 50% acetic acid (25 c.c.). The sulphonamide so obtained formed colourless plates, m. p. 251° (Found: C, 60·2; H, 4·3; N, 14·1. Calc. for $C_{15}H_{13}O_2N_3S$: C, 60·2; H, 4·4; N, 14·05%). Bobranski (*loc. cit.*) gives the m. p. as 251°, but Gray (*loc. cit.*) gives 261°. Repeated crystallisations, however, of the above product failed to raise the m. p. It was soluble in dilute caustic alkali solution, but gave an insoluble hydrochloride with 2N-hydrochloric acid. Diazo-coupling tests for free amino-group were negative.

p-(1′-iso*Quinolylamino*)*benzenesulphonamide*.—A mixture of 1-chloro*iso*quinoline (4·0 g.) and sulphanilamide (4·3 g.; 1 equiv.) was refluxed at 165° for 30 minutes. The mixture was dissolved in hot 2N-sodium hydroxide (70 c.c.) and, after filtration, was acidified with 50% acetic acid. The gum formed rapidly solidified; it weighed 7·3 g. (97%) and was crystallised by solution in alcohol (70 c.c.) mixed with 2N-hydrochloric acid (11 c.c.) at 70°, followed by addition of saturated sodium acetate solution to the filtered solution, p-(1′-iso*quinolylamino*)-*benzenesulphonamide* being obtained in colourless plates, m. p. 275° (sintering at 265°), soluble in 2N-sodium hydroxide and in 2N-hydrochloric acid but sparingly soluble in the usual organic solvents. Diazo-coupling tests showed absence of a free amino-group (Found: N, 14·0. $C_{15}H_{13}O_2N_3S$ requires N, 14·05%).

1-(p-*Aminobenzenesulphonamido*)iso*quinoline*.—This could not be obtained from 1-chloro-*iso*quinoline and sulphanilamide in the presence of potassium carbonate and copper. It was obtained by addition of *p*-acetamidobenzenesulphonyl chloride (16·0 g.) to a solution of 1-amino*iso*quinoline (9·7 g.) in pyridine (20 c.c.), the temperature being kept below 50°. Addition of water (350 c.c.) caused precipitation of a gum, which was induced to solidify with difficulty. Purified by solution in a mixture of alcohol (250 c.c.) and the required amount of 2N-sodium hydroxide at 70° and precipitation of the filtered solution at the b. p. with 2N-acetic acid, 1-(p-*acetamidobenzenesulphonamido*)iso*quinoline* (7·7 g.) was obtained in colourless prisms, m. p. 225° (Found: N, 12·2. $C_{17}H_{15}O_3N_3S$ requires N, 12·3%). When it was boiled with 2N-sodium hydroxide (10 c.c. per g.) for 1 hour and the mixture acidified with dilute acetic acid, 1-(p-*aminobenzenesulphonamido*)iso*quinoline* was obtained in tiny prismatic crystals, m. p. 263° (yield, 84%) (Found: N, 14·0. $C_{15}H_{13}O_2N_3S$ requires N, 14·05%). It was soluble in caustic alkalis and gave an insoluble crystalline hydrochloride with 2N-hydrochloric acid. It was practically insoluble in the ordinary solvents and gave an insoluble yellow diazo-compound, which coupled normally.

2-*Chloro-5-nitropyridine*.—Since the original work on the nitration of 2-aminopyridine is published by Tschitschibabin and his co-workers in Russian (*J. Russ. Phys. Chem. Soc.*, 1914, **46**, 1236; 1915, **47**, 1386; 1923, **55**, 471), the following details are given. 2-Aminopyridine (54 g.) was added with stirring to sulphuric acid (*d* 1·84, 240 c.c.) below 90°. The solution was cooled to 0°, and a cooled mixture of nitric acid (*d* 1·42, 39 c.c.) and sulphuric acid (*d* 1·84, 42 c.c.) added with stirring between 10° and 20°. The mixture was stirred for 1 hour further at 15° [if it is treated at this stage with ice, 2-nitroaminopyridine, m. p. 190° (decomp.), is obtained in 70% yield] and then warmed to 35°; the temperature rose spontaneously to about 65°. On addition of ice and water and basification with sodium carbonate (anhydrous) a mixture of 5- and 3-nitro-2-aminopyridines was formed, from which the two isomerides could be separated by a tedious fractionation from alcohol and acetone.* It is not necessary, however, to separate them in order to proceed to 2-chloro-5-nitropyridine. The wet mixture was estimated for water content; the nitration yield was usually about 70%. The equivalent of 59 g. of the dry mixture was dissolved in water (915 c.c.) by means of sulphuric acid (*d* 1·84, 63·6 c.c.), ice (250 g.) added,

* It is not prudent to isomerise larger batches of nitroaminopyridine; if larger nitrations are done, it is advisable to divide them into lots approximately equal to the above, to isomerise them separately, and to recombine them before working up.

followed by a solution of sodium nitrite (32·8 g.) in water (118 c.c.) with stirring. The stem of the dropping-funnel carrying the nitrite solution was arranged to dip below the surface of the reaction mixture and to feed near the point of maximum agitation. After the addition the mixture was stirred for 30 minutes, and the precipitated solid collected and washed with water. This proved to be nearly pure 5-nitro-2-hydroxypyridine, m. p. 180°. It did not depress the m. p. (184°) of a pure specimen made similarly from pure 5-nitro-2-aminopyridine (Tschitschibabin and Bylinkin, *J. Russ. Phys. Chem. Soc.*, 1914, **46**, 1236). The yield was 30 g.; a further 10 g. were obtained by concentration of the filtrate to about half bulk. The total yield was thus 66%. The fate of the isomeric 3-nitro-derivative has not yet been determined. The dry 5-nitro-2-hydroxypyridine (41·4 g.) was refluxed with phosphorus pentachloride (69·1 g.) and phosphorus oxychloride (4·1 c.c.) at 110° for 3 hours, the volatile phosphorus chlorides removed by distillation under reduced pressure, and the residue treated with ice. The mixture was ground, and the solid washed with water and dried at 90°, giving 2-chloro-5-nitropyridine (44·3 g.), m. p. 106° alone or mixed with an authentic specimen.

p-(5′-*Nitro*-2′-*pyridylamino*)*benzenesulphonamide*.—(1) A mixture of 2-chloro-5-nitropyridine (15·8 g.) with sulphanilamide (17·2 g.; 1 equiv.) was heated at 170° for 15 minutes. The solid cake was extracted with boiling 2N-sodium hydroxide, and the deep red solution acidified with dilute hydrochloric acid. Excess of saturated sodium acetate was then added, and the amorphous precipitate collected, washed with water, and boiled for a short time with alcohol (160 c.c.). The crystalline solid was collected, washed with 50% spirit, and dried (7·7 g., m. p. 204—206°). From the alcoholic filtrate a further crop (7·0 g.), m. p. 200—202°, was obtained after several days. The total yield of the *sulphonamide* was about 51%. Crystallised from 50% acetic acid, both fractions melted at 209—210° and were identical with the synthetic product described below (Found: N, 19·0. $C_{11}H_{10}O_4N_4S$ requires N, 9·0%).

(2) (a) *Sodium* p-(5′-*nitro*-2′-*pyridylamino*)*benzenesulphonate*. Anhydrous sulphanilic acid (35 g. or an equivalent amount of the hydrated acid) was dissolved in a solution of sodium hydroxide (8·0 g.) in water (100 c.c.). One equiv. (32 g.) of 2-chloro-5-nitropyridine was added, and the mixture refluxed for several hours, during which period a further amount of sodium hydroxide solution (8·0 g. in 50 c.c. of water) was added. The final reaction was alkaline to litmus but not to phenolphthalein. On cooling, the above sodium salt separated; it was drained on a porous tile, washed with alcohol and ether, and dried (36 g. Found for material crystallised from 2 parts of boiling water: Na, 7·5; N, 13·0. $C_{11}H_8O_5N_3SNa$ requires Na, 7·3; N, 13·1%). The procedure is based upon that given in E.P. 152,406 for the preparation of sodium 2 : 4-dinitrodiphenylamine-4-sulphonate. (b) p-(5′-*Nitro*-2′-*pyridylamino*)*benzenesulphonamide*. A mixture of the sodium salt from (a) (26 g.) with phosphorus pentachloride (17·3 g.) and phosphorus oxychloride (7·5 c.c.) was heated on a steam-bath for 45 minutes. The volatile phosphorus compounds were removed by distillation under reduced pressure, and the residue treated with ice. The moist sulphonyl chloride obtained was treated with aqueous ammonia (*d* 0·880, 70 c.c.), and the mixture heated on a steam-bath to remove the excess of ammonia. Dilution with water and addition of a little 2N-acetic acid gave the above sulphonamide (8·0 g.), m. p. 209—210° after crystallisation from 50% acetic acid (Found: N, 19·0%). The sulphonamide formed characteristic yellow rhombs, which gave a deep red solution in dilute aqueous sodium hydroxide. A faint pink colour with this reagent was discernible in dilutions as high as 1 in 10,000. It was insoluble in 2N-hydrochloric acid and incompletely soluble in 2N-ammonia (1 g. in 2 c.c.). Owing to the intense colour given in dilute sodium hydroxide solution, the diazo-coupling tests for free amino-group were indecisive.

p-(5′-*Amino*-2′-*pyridylamino*)*benzenesulphonamide*.—The nitro-compound (2·9 g., made by either of the above methods) was dissolved in 2N-sodium hydroxide (10 c.c.) and added at 60° to a suspension of ferrous hydroxide from crystallised ferrous sulphate (20·0 g.) in water (50 c.c.) and sodium hydroxide (5·6 g.) in water (15 c.c.). After filtration and neutralisation with dilute acetic acid the above *amine* was obtained. After solution in 2N-hydrochloric acid (charcoal) in the cold and neutralisation of the filtered solution with 25% aqueous sodium hydroxide, it formed pink needles, m. p. 221°, readily soluble in dilute caustic alkali solution and in dilute acetic and hydrochloric acids. Diazo-coupling tests were positive (Found: N, 21·1. $C_{11}H_{12}O_2N_4S$ requires N, 21·1%).

5-*Nitro*-2-(p-*aminobenzenesulphonamido*)*pyridine*.—(1) 2-Chloro-5-nitropyridine (15·8 g.) was mixed with *p*-acetamidobenzenesulphonamide (21·4 g.), potassium carbonate (anhydrous, 13·5 g.), and copper powder (1·0 g.) and heated at 180° for 1 hour. The mixture was extracted with hot water, and the filtered extract acidified with 2N-acetic acid. The 5-*nitro*-2-(p-*acetamidobenzenesulphonamido*)*pyridine* obtained (20·0 g.) was suspended in boiling alcohol (400 c.c.)

and dissolved by addition of 2N-sodium hydroxide; addition of boiling 50% acetic acid (100 c.c.) gave the acetyl derivative, m. p. 279° (Found: N, 16·4. $C_{13}H_{12}O_5N_4S$ requires N, 16·6%).

(2) The same compound (m. p. 277—279° when purified as above) was obtained by addition of *p*-acetamidobenzenesulphonyl chloride (5·6 g.) to a solution of 5-nitro-2-aminopyridine (3·2 g.) in pyridine (10 c.c.), followed by addition of cold N-hydrochloric acid when the somewhat vigorous reaction was over. It did not depress the m. p. of the product from (1) (Found: N, 16·5%).

The acetyl compound was boiled with 2N-sodium hydroxide (10 c.c. per g.) for 1 hour; acidification with acetic acid gave *5-nitro-2-(p-aminobenzenesulphonamido)pyridine*, m. p. 218—220° after crystallisation from 50% acetic acid (Found: N, 19·0. $C_{11}H_{10}O_4N_4S$ requires N, 19·0%).

(3) A mixture of 2-chloro-5-nitropyridine (8·0 g.), sulphanilamide (8·6 g.), potassium carbonate (7·0 g.), and copper powder (0·05 g.) was heated at 140° for 30 minutes. A vigorous reaction took place. The mixture was dissolved in boiling N-sodium hydroxide, filtered, and acidified with acetic acid, and the precipitate washed with water and dried (8·1 g., m. p. 190—200°. Found: N, 18·7%). This mixture was boiled for a few minutes with N-sodium hydroxide (11 c.c.) and, after cooling, the solution was filtered. The solid (A) weighed 9·6 g., melted at 214—215°, and did not depress the m. p. of genuine 5-nitro-2-(*p*-aminobenzenesulphonamido)-pyridine. It gave a pale red solution with dilute aqueous hydroxide. Mixed with *p*-(5′-nitro-2′-pyridylamino)benzenesulphonamide, it melted at 180—190°. After crystallisation from 50% acetic acid the m. p. rose to 218—220° and the substance appeared to be identical in all respects, including its characteristic crystalline form, with the synthetic product from (1) and (2), save that it gave a pale pink solution in dilute aqueous caustic soda (Found: N, 18·9%). Nesslerisation indicated this to contain 0·1—0·2% of the isomeric *p*-(5′-nitro-2′-pyridylamino)benzenesulphonamide, but further purification could not be effected.

The filtrate from the solid (A) was acidified with acetic acid, giving 5·95 g. of amorphous substance (B). This was digested with cold 2N-ammonia (10 c.c.), and the liquid filtered. The insoluble solid was re-treated with cold N-ammonia (5 c.c.) and then, on repeated crystallisation from 50% acetic acid and finally from 95% alcohol, had m. p. 208—209°, gave a deep red solution in dilute aqueous sodium hydroxide, and did not depress the m. p. of synthetic *p*-(5′-nitro-2′-pyridylamino)benzenesulphonamide (Found: N, 19·1%). A mixture with its isomeride, however, melted at 180—190°. The ammoniacal filtrate from this on acidification with acetic acid gave 3·2 g. of crude 5-nitro-2-(*p*-aminobenzenesulphonamido)pyridine, identified as above. A similar mixture of the two isomerides was obtained from 2-chloro-5-nitropyridine, the sodium salt of sulphanilamide (1 equiv.), potassium carbonate (0·5 mol.), and a trace of copper under similar conditions.

5-Nitro-2-(*p*-aminobenzenesulphonamido)pyridine forms stout yellow polyhedra of characteristic shape, m. p. 218—220°, gives yellow solutions in dilute aqueous sodium hydroxide and ammonia, and is insoluble in dilute mineral acids and in the ordinary organic solvents. The diazo-coupling reactions show the presence of a free amino-group.

5-Amino-2-(p-aminobenzenesulphonamido)pyridine.—The nitro-compound obtained by any of the above methods (54 g.) was mixed with reduced iron powder (32 g.) and added to a boiling solution of acetic acid (32 c.c.) in water (800 c.c.). After boiling for 20 minutes, the mixture was neutralised with 2N-ammonia and the solution was filtered and acidified with 50% acetic acid. The crystalline solid obtained, presumably 5-amino-2-(*p*-acetamidobenzenesulphonamido)pyridine, was washed, dried (yield, 6 g.), and boiled with 60 c.c. of 2N-sodium hydroxide for 1 hour. Acidification with 50% acetic acid then gave a 50% yield of *5-amino-2-(p-aminobenzenesulphonamido)pyridine*. This crystallised from 50% alcohol in colourless needles, which turned pink on exposure to air; it was readily soluble in dilute caustic alkalis and in mineral acids. The diazo-solution was yellow and coupled normally. The amine had no definite m. p. but sintered at 140—150° and was not completely molten at 200° (Found: N, 21·1. $C_{11}H_{12}O_2N_4S$ requires N, 21·1%).

p-(2′-Pyridylamino)benzenesulphon-2′-pyridylamide.—A mixture of *p*-(2′-pyridylamino)-benzenesulphonamide (6·25 g.) with 2-bromopyridine (4·0 g.), potassium carbonate (3·5 g.), and copper powder (0·05 g.) was refluxed for 1 hour. The product was dissolved in boiling water (150 c.c.), filtered from copper, and acidified with dilute acetic acid, giving 5·5 g. of a product, m. p. 185—190°. This was dissolved in a mixture of boiling alcohol (37 c.c.) and 2N-sodium hydroxide (25 c.c.) and acidified with excess of boiling 2N-acetic acid. *p-(2′-Pyridylamino)benzenesulphon-2′-pyridylamide* so obtained formed colourless needles, m. p. 204°, soluble in dilute caustic alkalis and mineral acids and sparingly soluble in the ordinary organic solvents

(Found: N, 17·2. $C_{16}H_{14}O_2N_4S$ requires N, 17·1%). Attempts to prepare this compound from 2-(*p*-aminobenzenesulphonamido)pyridine and 2-bromo- or 2-iodo-pyridine by Bobranski's method (*loc. cit.*) failed, the unchanged pyridylamide being recovered in each case in good yield.

The author wishes to express his gratitude to Dr. A. J. Ewins, under whose guidance the above work was done, to Mr. S. Bance for the semi-microanalyses recorded, and to the Directors of Messrs. May and Baker, Ltd., for permission to publish the results.

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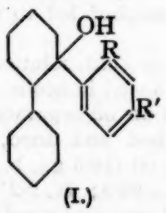
4. 1-*Methoxy- and* 2-*Methoxy-triphenylene.*

By W. S. RAPSON.

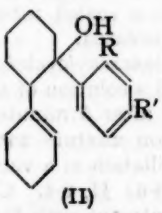
A convenient synthesis of triphenylene derivatives is described. 2-*cyclo*Hexenyl-*cyclo*hexanone is condensed with an arylmagnesium halide, and the product cyclised by the action of stannic chloride or aluminium chloride. Disproportionation accompanies cyclisation, since an octahydrotriphenylene, which can be separated as its picrate, is the best-defined product of the reaction. The corresponding triphenylene is produced from the octahydrotriphenylene by dehydrogenation. Triphenylene itself, 2-methyltriphenylene, and 1- and 2-*methoxytriphenylenes* have been prepared by this method—the last substances to act as reference compounds in the orientation of other substituted triphenylenes.

RELATIVELY few modes of entry into the triphenylene series have been worked out, and apart from 1- and 2-methyltriphenylenes (Fieser and Joshel, *J. Amer. Chem. Soc.*, 1939, **61**, 2958; Bachmann and Struve, *J. Org. Chem.*, 1939, **4**, 472) no reference substances are available for the orientation of substituted triphenylenes. The syntheses of 1-*methoxytriphenylene* and 2-*methoxytriphenylene* described here began from the observation by Nenitzescu and Curcaneanu (*Ber.*, 1937, **70**, 346) that 1-phenyl-2-*cyclo*hexyl*cyclo*hexanol (I; R = R′ = H) could be dehydrogenated by selenium in a sealed tube to yield triphenylene. The experiments of these authors have been repeated, but it has only been possible to confirm the small yields recorded by them. Under similar conditions no characterisable products could be obtained from 1-*p*-methoxyphenyl-2-*cyclo*hexyl*cyclo*hexanol (I; R = H, R′ = OMe) or from 1-*o*-methoxyphenyl-2-*cyclo*hexyl*cyclo*hexanol (I; R = OMe, R′ = H).

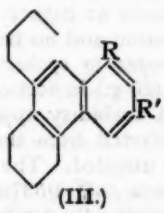
The dehydrogenation of 1-phenyl-2-*cyclo*hexenyl*cyclo*hexanol (II; R = R′ = H), prepared by the interaction of phenylmagnesium bromide and 2-*cyclo*hexenyl*cyclo*hexanone, was therefore explored. This could be made to yield triphenylene in small amounts only, and when the similar dehydrogenation of 1-*p*-methoxyphenyl-2-*cyclo*hexenyl*cyclo*hexanol (II; R = H, R′ = OMe) was carried out, the only product isolated was a trace of 2-*hydroxytriphenylene*. The cyclisation of (II, R = R′ = H) was therefore attempted as a



(I.)



(II)



(III.)

preliminary to its dehydrogenation. Sulphuric acid in acetic acid effected only its dehydration—presumably to 1-*phenyl*-2-cyclo*hexenyl*cyclo*hexene*—since only small yields of triphenylene were formed from the product on dehydrogenation. Both stannic chloride and aluminium chloride, however, gave rise to a mixture of products from which much greater yields of triphenylene were obtained on dehydrogenation. The mixture could

be separated with the aid of picric acid into a crystalline substance, formulated as 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-*octahydrotriphenylene* (III; R = R′ = H), and a liquid material, from which triphenylene was formed in appreciable amount on dehydrogenation but nothing homogeneous could be isolated.

A similar series of reactions beginning with 1-*p*-tolyl-2-*cyclo*hexenyl*cyclo*hexanol (II; R = H, R′ = Me) led to 2-methyltriphenylene, and from the appropriate starting materials (II; R = H, R′ = OMe) and (II; R = OMe, R′ = H), 2-methoxytriphenylene and 1-methoxytriphenylene were prepared. In the latter syntheses aluminium chloride was preferable to stannic chloride as cyclising agent, since the latter effected slight chlorination. 2-Methoxytriphenylene has been demethylated to yield 2-hydroxytriphenylene, but 1-methoxytriphenylene offered considerable resistance to demethylation.

Experimental.

2-cyclo*Hexenyl*cyclo*hexanone*.—The following procedure is an improvement on the methods described by Mannich (*Ber.*, 1907, **40**, 154) and by Wallach (*ibid.*, p. 70; *Annalen*, 1911, **381**, 97). *cyclo*Hexanone was saturated with dry hydrogen chloride at room temperature (water cooling) and left overnight. The mixture, which solidified owing to the formation of the hydrochloride of 2-*cyclo*hexenyl*cyclo*hexanone, was warmed and shaken vigorously after addition of sodium hydroxide or pyridine in excess. After 2 hours the upper layer was separated, washed with water, dried, and distilled in a vacuum, giving an almost quantitative yield of 2-*cyclo*hexenyl*cyclo*hexanone, b. p. 142—145°/15 mm.

2-cyclo*Hexyl*cyclo*hexanone* (compare Wallach, *Annalen*, 1911, **381**, 95).—A palladium–strontium carbonate catalyst (10 g.) was added to a mixture of 2-*cyclo*hexenyl*cyclo*hexanone (40 g.) and alcohol (40 c.c.), which was then shaken with hydrogen at 1·5 atms.; reaction was complete in 15 minutes. The alcohol was evaporated from the filtered solution, and the residue distilled in a vacuum, giving 2-*cyclo*hexyl*cyclo*hexanone, b. p. 136—140°/11 mm.

The Action of Anisylmagnesium Bromide on 2-cyclo*Hexyl*cyclo*hexanone*.—Anisylmagnesium bromide (from 20 g. of *p*-bromoanisole), reacting with 2-*cyclo*hexyl*cyclo*hexanone (18 g.) in the usual way, gave a viscous oil (10 g.), which distilled at 205—210°/5 mm., some decomposition (dehydration) occurring. It crystallised slowly, but was not obtained analytically pure. When it was heated with selenium (17 g.) at 300—320° for 36 hours, dehydration and evolution of hydrogen selenide occurred, but no crystalline material could be isolated from the product obtained by vacuum distillation.

1-*Phenyl*-2-cyclo*hexenyl*cyclo*hexanol* (II; R = R′ = H).—2-*cyclo*Hexenyl*cyclo*hexanone (59 g.) was added to an ethereal solution of phenylmagnesium bromide prepared from bromobenzene (53 g.). Reaction was completed by warming on the water-bath for 1 hour, and after addition of dilute sulphuric acid and ice the ethereal layer was separated. It yielded a product (57 g.), b. p. 170—175°/3 mm., $n_D^{26°}$ 1·5485 (Found: C, 84·4; H, 9·7. Calc. for $C_{18}H_{24}O$: C, 84·4; H, 9·4%), which did not react with 2 : 4-dinitrophenylhydrazine. In an attempted dehydrogenation it was mixed (7 g.) with selenium (10 g.) and heated at 320—340° for 36 hours. On distillation a product (5 g.) was obtained which crystallised partly on cooling. The crystals were separated by the addition of methyl alcohol and filtration, and were identified as triphenylene (0·3 g.). The filtrate was returned to the dehydrogenation flask, the solvent evaporated, and the heating with selenium continued for 24 hours. After working up as before, a further small yield of triphenylene was isolated. No improvement in yield was effected in experiments at higher temperatures in a sealed tube. The use of sulphur led to extensive resinification and no triphenylene was isolated.

Attempts to cyclise 1-*Phenyl*-2-cyclo*hexenyl*cyclo*hexanol*.—(a) To a cold solution of the alcohol (20 g.) in acetic acid was added a solution of sulphuric acid (15 c.c.) in acetic acid (150 c.c.). A turbidity appeared suddenly after 5 minutes' shaking, and an oil separated. This was extracted from the diluted reaction mixture with benzene, washed, and dried, and the benzene distilled. The residue on distillation in a vacuum yielded an oil (16·5 g.), b. p. 155—160°/4 mm., $n_D^{26°}$ 1·5670 (Found: C, 90·6; H, 9·4. $C_{18}H_{22}$ requires C, 90·8; H, 9·2%). The yield was rapidly diminished if the treatment with the sulphuric acid was prolonged or if the reaction mixture was heated. This oil (13 g.) yielded triphenylene (1·5 g.) after repeated treatment with selenium.

(b) The alcohol (25 g.) was dissolved in carbon disulphide (75 c.c.) and added to aluminium chloride (26 g.) suspended in carbon disulphide (75 c.c.) and cooled in ice. A bright viole complex formed gradually as the mixture was shaken and allowed to come to room temperature.

After 5 hours, ice and dilute hydrochloric acid were added and, when the complex had decomposed, the carbon disulphide layer was separated, the carbon disulphide evaporated, and the residue distilled in a vacuum. A distillate (15 g.) was collected, b. p. 180—250°/4 mm., the later portions of which crystallised. It was dissolved in the minimum quantity of acetic acid, and a hot solution of picric acid (9 g.) in acetic acid added. A red picrate separated (9 g.), which, recrystallised from acetic acid, formed needles, m. p. 185°. It was decomposed with ammonia, yielding a white crystalline hydrocarbon, which formed prisms, m. p. 129—130°, after recrystallisation from acetic acid (Found: C, 91·2; H, 8·3. $C_{18}H_{20}$ requires C, 91·5; H, 8·5%). It is formulated as 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-*octahydrotriphenylene*, since on heating at 300° for 2 hours with a palladium–charcoal catalyst it gave an almost quantitative yield of triphenylene. Dehydrogenation with sulphur also gave good yields of triphenylene, but in a crude form difficult to purify. The same difficulty has been observed with the products of other sulphur dehydrogenations in this series.

The filtrate from the picrate above was diluted with water and extracted with ether; the extracts, after being washed free from picric acid with alkali, yielded a liquid product (9 g.), b. p. 175—185°/4 mm. Nothing homogeneous could be separated from it, but it yielded triphenylene (2·5 g.) and oily by-products on catalytic dehydrogenation.

(c) Similar results were obtained when stannic chloride was used in place of aluminium chloride in the experiments above.

2-*Methyltriphenylene* (with E. Rollnick).—This was prepared in exactly the same way as triphenylene itself, the initial materials being *p*-tolylmagnesium bromide and 2-*cyclo*hexenyl-*cyclo*hexanone. 2-*Methyl*-5 : 6 : 7 : 8 : 9 : 10 : 11 : 12-*octahydrotriphenylene* was recrystallised from aqueous alcohol, forming plates, m. p. 93—94° (Found: C, 91·5; H, 8·4. $C_{19}H_{22}$ requires C, 91·2; H, 8·8%). Its picrate, recrystallised from acetic acid, formed red needles, which melted after slight sintering at 195·5°. It yielded 2-methyltriphenylene, m. p. 102°, on dehydrogenation with a palladium–charcoal catalyst.

1-*Methoxytriphenylene*.—Reaction between 2-*cyclo*hexenyl*cyclo*hexanone and *o*-methoxyphenylmagnesium bromide (from 40 g. of *o*-bromoanisole) was effected in the usual way, and the product worked up by vacuum distillation. The product (35 g.), b. p. 188—192°/6 mm., crystallised with extreme slowness and was so difficult to recrystallise that it was not obtained in an analytically pure condition. It failed to react with ketonic reagents, and after treatment with selenium at 320—340° for 48 hours no characteristic product was obtained. It was dissolved (30 g.) in carbon disulphide (100 c.c.) and added with shaking to an ice-cooled suspension of aluminium chloride (25 g.) in carbon disulphide (100 c.c.). The mixture was allowed to warm to room temperature; after 4 hours, dilute hydrochloric acid and ice were added and, when the solid red complex had been decomposed, the carbon disulphide layer was separated, and dried, and the carbon disulphide evaporated. On distillation of the residue in a vacuum a product was obtained (23 g.), b. p. 190—260°/4 mm., the greater part at 194—200°, which partly crystallised, especially the higher-boiling fractions. The deep brown picrate, prepared from an acetic acid solution, was decomposed by solution in pyridine, followed by addition of water, giving 1-*methoxy*-5 : 6 : 7 : 8 : 9 : 10 : 11 : 12-*octahydrotriphenylene*, which, recrystallised from acetic acid, formed flat rhombohedral prisms (8 g.), m. p. 96—97° (Found: C, 85·2; H, 8·1. $C_{19}H_{22}O$ requires C, 85·7; H, 8·3%). Its picrate crystallised from acetic acid in deep brown needles, m. p. 204—205°. 1-*Methoxytriphenylene* was formed almost quantitatively when the above substance (2 g.) was mixed with a 20% palladium–charcoal catalyst (0·2 g.) and heated at 300° for 2 hours; it was sparingly soluble in the majority of solvents, and was recrystallised from aqueous pyridine or from dioxan, separating in plates, m. p. 172° (Found: C, 88·2; H, 5·5. $C_{19}H_{14}O$ requires C, 88·4; H, 5·4%). Its picrate dissociated with great ease, but separated when a saturated solution of 1-methoxytriphenylene in methyl alcohol was treated with picric acid, forming orange needles, m. p. 196—198°. 1-Methoxytriphenylene was unaffected after boiling for 10 hours with hydriodic acid (*d* 1·7), and even after addition of acetic acid to the reaction mixture and further prolonged boiling, only traces of phenolic material could be isolated.

The mother-liquor from the picrate of (III; R = OMe, R′ = H) was diluted with water and extracted with ether, and the extracts freed from picric acid by shaking with sodium hydroxide solution. The ether was then evaporated and on distillation of the residue in a vacuum a fraction, b. p. 190—200°, was collected. It yielded further small amounts of 1-methoxytriphenylene on dehydrogenation, along with non-crystalline material which was not identified.

2-*Methoxytriphenylene*.—Anisylmagnesium bromide and 2-*cyclo*hexenyl*cyclo*hexanone

yielded in the usual way a non-ketonic product, b. p. 193—197°/7 mm. It was a viscous oil which showed signs of decomposition during distillation and did not crystallise even after long standing. No characterisable products were obtained from it by treatment with selenium at 320—350°, but after 12 hours' heating in a sealed tube at 340° a trace of crystalline material was isolated by treating the viscous oil which constituted the bulk of the product with ether–light petroleum. This separated from aqueous methyl alcohol in white needles, m. p. 214° after sintering at 212°. It was later identified as slightly impure 2-*hydroxytriphenylene* (Found : C, 89·1; H, 4·7. $C_{18}H_{12}O$ requires C, 88·5; H, 4·9%).

The distilled product of the Grignard reaction above (25 g.) was dissolved in carbon disulphide (50 c.c.) and added to an ice-cooled suspension of aluminium chloride (25 g.) in carbon disulphide (50 c.c.). The procedure described under 1-methoxytriphenylene was then followed and the distillate, b. p. 190—260°/4 mm., obtained from the material in the carbon disulphide layer was converted into a bright red picrate. This was decomposed, giving 2-*methoxy*-5 : 6 : 7 : 8 : 9 : 10 : 11 : 12-*octahydrotriphenylene*, which, recrystallised from slightly aqueous acetic acid, formed flat elongated prisms (8 g.), m. p. 120—121° (Found : C, 85·3; H, 8·0. $C_{19}H_{22}O$ requires C, 85·7; H, 8·3%). Its picrate was recrystallised from acetic acid, forming brick-red needles, m. p. 193—194°.

2-Methoxy-5 : 6 : 7 : 8 : 9 : 10 : 11 : 12-octahydrotriphenylene (2 g.) was heated with a 30% palladium–charcoal catalyst at 300°. After 3 hours the evolution of hydrogen had ceased, and the 2-*methoxytriphenylene* was taken up in acetone, decolorised with charcoal, and precipitated by the addition of water. It was recrystallised by solution in acetone or pyridine, followed by addition of water; the emulsion initially formed rapidly set to a felted mass of needles, m. p. 97—98° (Found : C, 88·4; H, 5·6. $C_{19}H_{14}O$ requires C, 88·4; H, 5·4%).

2-*Hydroxytriphenylene*.—2-Methoxytriphenylene (2 g.) was boiled with a mixture of hydriodic acid (*d* 1·7, 8 c.c.) and acetic acid (4 c.c.) for 3 hours. The reaction mixture was poured into sodium sulphite solution, and ether added. 2-Hydroxytriphenylene was extracted from the ethereal layer with N-sodium hydroxide and precipitated from this solution with acid. It was recrystallised by solution in hot alcohol, followed by the judicious addition of water; it separated, on cooling, in small slender prisms, m. p. 213—215° (after previous sintering) (Found : C, 88·2; H, 5·1. Calc. for $C_{18}H_{12}O$: C, 88·5; H, 4·9%).

2-*Acetoxytriphenylene*, recrystallised from acetic acid, formed long slender prisms of rectangular outline, m. p. 129° (Found : C, 83·8; H, 4·9. $C_{20}H_{14}O_2$ requires C, 83·9; H, 4·9%).

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5. *Polycyclic Aromatic Hydrocarbons. Part XXVII.*

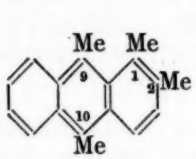
By G. M. BADGER, F. GOULDEN, and F. Ll. WARREN.

9 : 10-Dimethyl-9 : 10-dihydro-1 : 2-benzanthraquinol and 9 : 10-dimethyl-9 : 10-dihydro-1 : 2 : 5 : 6-dibenzanthraquinol have been dehydrated to endo-*oxides*, which are easily reduced to the completely aromatic hydrocarbons. This reaction furnishes an alternative route to the highly carcinogenic 9 : 10-dimethyl-1 : 2-benzanthracene. Unsuccessful attempts have been made to transform 1 : 2 : 9 : 10-tetramethyl-9 : 10-dihydroanthraquinol into 1 : 2 : 9 : 10-tetramethylanthracene (I).

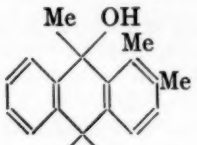
Two unsuccessful attempts to synthesise 1 : 2 : 9 : 10-tetramethylanthracene (I) have been recorded (Badger, Cook, and Goulden, J., 1940, 16; Fieser and Webber, *J. Amer. Chem. Soc.*, 1940, **62**, 1360). Our interest in this unknown hydrocarbon, which lies in its relationship to the actively carcinogenic 9 : 10-dimethyl-1 : 2-benzanthracene and the feebly carcinogenic 9 : 10-dimethylanthracene, has led us to renew our efforts to prepare it.

Reduction of 1 : 2 : 9 : 10-tetramethyl-9 : 10-dihydroanthraquinol (II) with hydriodic acid in acetic acid, a procedure whereby Cook (J., 1931, 495) prepared *meso*-dialkyl and -diaryl derivatives of 1 : 2 : 5 : 6-dibenzanthracene, gave a yellow amorphous product. Cook found that dihydroanthraquinols of the dibenzanthracene series were reduced to dihydrides of the aromatic hydrocarbons by hydriodic acid and red phosphorus in acetic acid. With the diol (II) this reaction led to the formation of a crystalline *compound* having the composition of 1 : 2 : 9 : 10-tetramethyl-9 : 10-dihydroanthracene, and its ultra-

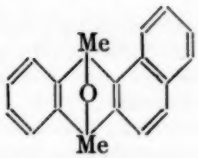
violet absorption spectrum, examined by Dr. E. Roe, is consistent with the formulation of a dihydroanthracene derivative. However, dehydrogenation to 1 : 2 : 9 : 10-tetramethylanthracene could not be accomplished.



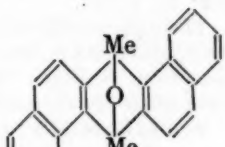
(I.)



(II.)



(III.)



(IV.)

For comparison, 9 : 10-*dimethyl*-9 : 10-*dihydroanthracene* was prepared, and its dehydrogenation examined. 9 : 10-Dimethylanthracene was smoothly formed when the dihydride was heated with sulphur at 230°. 9 : 10-Dimethylanthracene, and not its dihydride, was obtained when 9 : 10-dimethyl-9 : 10-dihydroanthraquinol was reduced with hydriodic acid and phosphorus in acetic acid. The dihydro-compound required for the dehydrogenation experiment was obtained by the action of methyl iodide on the disodio-compound of anthracene, a method introduced by Hugel and Lerer (*Bull. Soc. chim.*, 1933, **53**, 1498).

In the case of *meso*-dialkyldihydroanthraquinols loss of two molecules of water may occur following treatment with acetic acid containing a trace of mineral acid. However, Enderlin (*Compt. rend.*, 1936, **202**, 1188) obtained an endocyclic oxide by thermal dehydration of 1 : 10-diphenyl-4 : 9-bis-*p*-bromophenyl-9 : 10-dihydro-2 : 3-benzanthraquinol. Conditions have now been found for the facile monodehydration of 9 : 10-dimethyl-9 : 10-dihydro-1 : 2-benzanthraquinol and 9 : 10-dimethyl-9 : 10-dihydro-1 : 2 : 5 : 6-dibenzanthraquinol to compounds which are doubtless endo-*oxides* (III and IV). These oxides were reduced, the former by hydriodic acid and the latter by methylmagnesium iodide, to the 9 : 10-dimethyl derivatives of 1 : 2-benzanthracene and 1 : 2 : 5 : 6-dibenzanthracene, respectively.

Experimental.

1 : 2 : 9 : 10-*Tetramethyl*-9 : 10-*dihydroanthracene*.—A Grignard solution was prepared from methyl iodide (2·5 c.c.), magnesium (0·9 g.), ether (15 c.c.), and benzene (15 c.c.), most of the ether distilled off on the water-bath, and benzene (15 c.c.) added. 1 : 2-Dimethylanthraquinone (2·3 g.) (Badger, Cook, and Goulden, *loc. cit.*), suspended in a Soxhlet thimble underneath the condenser (compare Bachmann and Chemerda, *J. Org. Chem.*, 1939, **4**, 583), dissolved after the solution had been refluxed for 4 hours. After decomposition with ice-cold ammonium chloride solution, the organic layer was evaporated, and the resulting oil boiled in acetic acid (50 c.c.) with red phosphorus (1·5 g.) and hydriodic acid (5 c.c., *d* 1·9) for 2 hours and poured into water. An alcoholic solution of the solid was decolourised with charcoal and evaporated to small volume. The *product*, probably 1 : 2 : 9 : 10-tetramethyl-9 : 10-dihydroanthracene, formed colourless needles (0·9 g.), m. p. 100—101°, from alcohol (Found : C, 91·4; H, 8·35. $C_{18}H_{20}$ requires C, 91·45; H, 8·55%).

Dehydrogenation with sulphur at 230° for ½ hour gave a product which decomposed on attempted distillation. In another experiment, 1 g. of the dihydro-compound was heated at 265° for ½ hour with a palladium catalyst (0·2 g.). The product was extracted with acetic acid, the solution concentrated (a portion of it did not give a coloration with picric acid), and a few drops of water added. The yellow amorphous precipitate decomposed at 130° and could not be crystallised (Found : C, 92·25; H, 7·6. $C_{18}H_{18}$ requires C, 92·3; H, 7·7%).

9 : 10-*Dimethylanthracene*.—(i) A solution of 9 : 10-dihydroxy-9 : 10-dimethyl-9 : 10-dihydroanthracene (2 g.) (Bachmann and Chemerda, *J. Org. Chem.*, 1939, **4**, 583) in acetic acid (100 c.c.) was treated with red phosphorus (3 g.) and hydriodic acid (5 c.c., *d* 1·9) and boiled for 2 hours. The reaction mixture was worked up as above. After sublimation at 110°/0·2 mm., and recrystallisation from benzene, the product (0·45 g.) formed pale yellow crystals, m. p. 180—181°, alone or mixed with authentic 9 : 10-dimethylanthracene.

(ii) A suspension of anthracene (40 g.), powdered sodium (20 g.), and broken glass in ether (400 c.c.) was shaken for 48 hours. A blue colour developed after the first ½ hour and gradually became very intense. The mixture was cooled in ice, and methyl iodide added dropwise through a reflux condenser until the solution had become decolourised. After filtration, the ether was evaporated, and the residue cooled in a freezing mixture. The unchanged anthracene which

crystallised was removed, and the filtrate distilled. The fraction (16 g.), b. p. 180—185°/25 mm., solidified and was recrystallised from alcohol, the pure 9 : 10-*dimethyl*-9 : 10-*dihydroanthracene* forming colourless crystals, m. p. 101—102° (Found : C, 92·0; H, 7·9. $C_{16}H_{16}$ requires C, 92·3; H, 7·7%).

The above dihydro-compound (3·3 g.) was heated at 230° for ½ hour with sulphur (0·55 g.). The product (2·8 g.) was purified through the picrate (m. p. 173—175°) and finally by recrystallisation from benzene. It formed pale yellow blades, m. p. 180—182°, alone or mixed with authentic 9 : 10-dimethylanthracene.

9 : 10-*Dimethyl*-9 : 10-*dihydro*-1 : 2-*benzanthracene* 9 : 10-*Oxide*.—This oxide was obtained by a method similar to that described by Bachmann and Chemerda (*J. Amer. Chem. Soc.*, 1938, **60**, 1023) for the preparation of 9 : 10-dimethoxy-9 : 10-dimethyl-9 : 10-dihydro-1 : 2-benzanthracene. A solution of 9 : 10-dihydroxy-9 : 10-dimethyl-9 : 10-dihydro-1 : 2-benzanthracene (10 g.) in benzene (30 c.c.) and methyl alcohol (40 c.c.) was warmed and then treated with concentrated sulphuric acid (0·5 c.c.). After several hours, the methyl ether which had crystallised was removed, and the filtrate evaporated to small volume, giving 9 : 10-*dimethyl*-9 : 10-*dihydro*-1 : 2-*benzanthracene* 9 : 10-*oxide* (5·5 g.), which, recrystallised from benzene, formed plates, m. p. 120—121° (Found : C, 88·2; H, 6·3. $C_{20}H_{16}O$ requires C, 88·2; H, 5·9%).

Reduction of the oxide. A solution of the oxide (11 g.) in glacial acetic acid (150 c.c.), at 30°, was treated with a solution of hydriodic acid (11 c.c., *d* 1·9) in acetic acid (20 c.c.). The mixture was shaken for a few minutes and then boiled for 10 minutes. Sulphur dioxide was passed into the slightly diluted solution in order to decolorise it; the hydrocarbon which crystallised was recrystallised from acetic acid (yield, 7 g.). It formed plates, m. p. 122° alone or mixed with authentic 9 : 10-dimethyl-1 : 2-benzanthracene but depressed by the original oxide.

9 : 10-*Dimethyl*-9 : 10-*dihydro*-1 : 2 : 5 : 6-*dibenzanthracene* 9 : 10-*Oxide*.—A solution of 9 : 10-dimethyl-9 : 10-dihydro-1 : 2 : 5 : 6-dibenzanthraquinol (1·4 g.) and picric acid (2·8 g.) in absolute alcohol (280 c.c.) was refluxed for 2 hours. After concentration, the picrate which separated was collected and dissociated by treatment with boiling alcohol, the *oxide* (1·0 g.) separating on cooling. Recrystallisation from *cyclo*hexane and from alcohol gave pale yellow needles, m. p. 140—141° (Found : C, 89·0; H, 6·1. $C_{24}H_{18}O$ requires C, 89·4; H, 5·6%).

The *picrate*, prepared from the pure oxide, formed deep red needles, m. p. 107—108° (Found : C, 65·5; H, 4·2. $C_{24}H_{18}O,C_6H_3O_7N_3$ requires C, 65·3; H, 3·8%).

Action of methylmagnesium iodide. The oxide (0·5 g.) was added to a Grignard solution prepared from methyl iodide (1 c.c.), magnesium (0·4 g.), and ether (10 c.c.). The orange-red solution was boiled for 2 hours and decomposed with ice and ammonium chloride, and the product recrystallised from benzene. The pale yellow leaflets gave an intense reddish-purple solution in concentrated sulphuric acid, and had m. p. 208—210°, not depressed by authentic 9 : 10-dimethyl-1 : 2 : 5 : 6-dibenzanthracene (J., 1931, 495) (Found : C, 93·5; H, 5·8. Calc. for $C_{24}H_{18}$: C, 94·1; H, 5·9%).

Our thanks are due to Professor J. W. Cook, F.R.S., for his interest in this work, to the Finney-Howell Research Foundation, Inc., and to the Sir Halley Stewart Trust for grants awarded to two of us (G. M. B. and F. Ll. W.), and to the British Empire Cancer Campaign for a grant to the Hospital.

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6. *Studies in the Light Absorption of Organic Compounds. Part IX. Unsaturated Carbonyl Compounds and Semicarbazones.*

By A. BURAWOY.

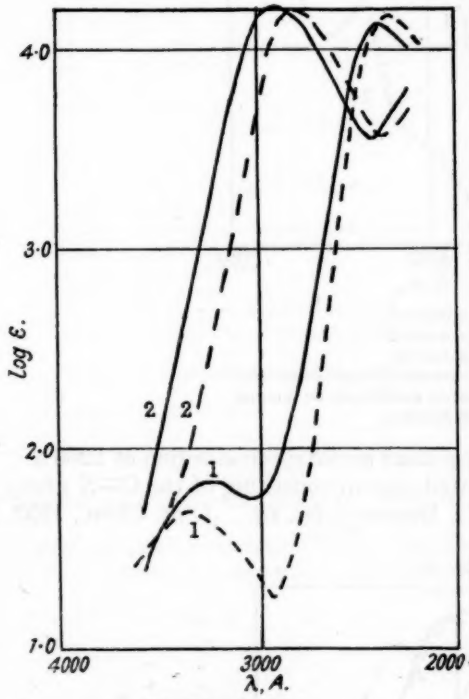
The absorption spectra of numerous aldehydes and ketones and their semicarbazones are discussed.

DURING attempts to determine the structure of vitamin-*A* and to synthesise it (Heilbron *et al.*, J., 1937, 755; 1939, 1554, 1556), it was necessary to rely on spectroscopic data for confirmation of purely chemical evidence regarding the structures of many of the compounds synthesised and their purity. The absorption spectra of a series of related compounds were therefore investigated in order to obtain relevant data, and the absorption

maxima and molecular extinction coefficients of these compounds are recorded in the table. The plots of λ against log ε are supplementary to those of Heilbron *et al.* (*locc. cit.*). The determinations were carried out with a Hilger E3 quartz spectrograph fitted with a Spekker photometer, a tungsten-steel high-tension spark being employed as the source of light.

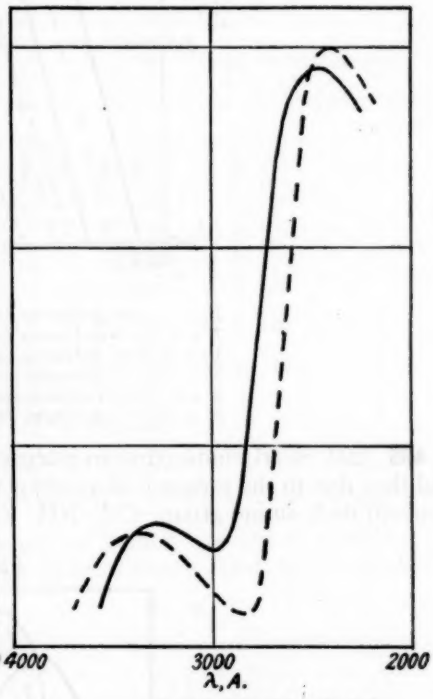
Citral (I, $n = 0$) and β-*cyclo*citral (II), like all αβ-unsaturated carbonyl compounds, exhibit two absorption bands, one of low intensity due to the carbonyl group and the other of high intensity due to the conjugated system present (Figs. 1 and 2). Comparison of the spectra in hexane and alcohol shows that in hexane the latter band is displaced to shorter and the former band to longer wave-lengths, thus confirming their attribution to the two different types of chromophoric groups appearing in organic compounds, *viz.*, (i) unsaturated atoms of free radicals, and all multiple linkages (*R*-chromophores, *R*-bands); (ii) conjugated

FIG. 1.



1 ——— *Citral in alcohol.*
1 - - - - - *Citral in hexane.*
2 ——— *Citrylideneacetaldehyde in alcohol.*
2 - - - - - *Citrylideneacetaldehyde in hexane.*

FIG. 2.



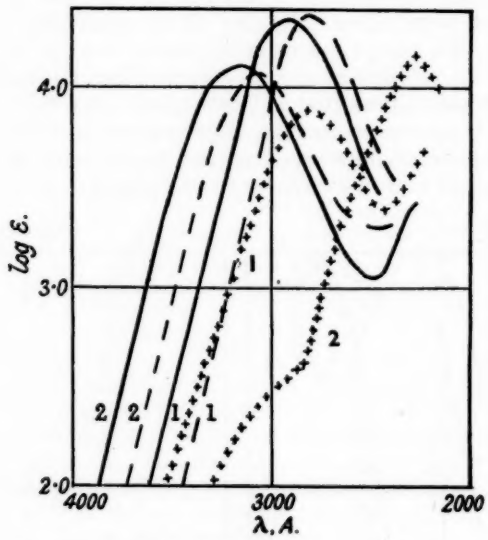
——— β-cyclo*Citral in alcohol.*
- - - - - β-cyclo*Citral in hexane.*

systems (*K*-chromophores, *K*-bands) (Burawoy, *Ber.*, 1930, **63**, 3155; 1931, **64**, 467; J., 1937, 1865; 1939, 1177).

The spectra of citrylideneacetaldehyde (I, $n = 1$), ψ-ionone (III), β-ionone (IV), and citrylidenecrotonaldehyde (I, $n = 2$) (Figs. 1 and 3) show that: (i) The intensive bands are displaced to longer wave-lengths with increasing length of the chromophoric conjugated system, but contrary to usual experience, the extinction coefficient of (I, $n = 2$) is smaller than those of both (I, $n = 0$) and (I, $n = 1$). The low-intensity band due to the carbonyl group is no longer detectable, since the additional ethenoid linkages, being only indirectly connected with this group, have only a small effect on this band, which is consequently superimposed by the high-intensity band. (ii) Ring closure is accompanied by a decrease in the intensity of the bands, but their relative positions remain unchanged. The intensity of the *K*-band of α-ionone (V), however, is of the same order as those of the open-chain compounds, since here, in contrast to β-*cyclo*citral and β-ionone, the double bond in the ring is not part of the chromophoric conjugated system.

In addition to the free carbonyl compounds, their semicarbazones have also been examined. Acetonesemicarbazone shows rising absorption (Menschik *et al.*, *Annalen*,

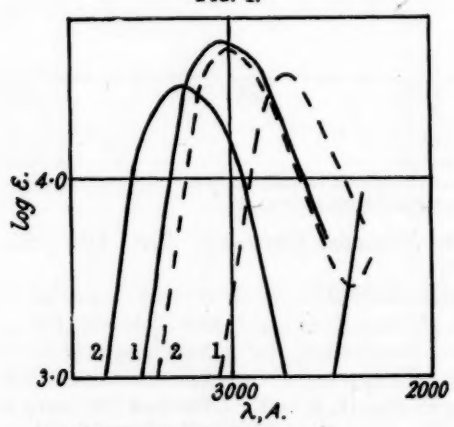
FIG. 3.



1 ——— *ψ-Ionone in alcohol.*
1 – – – – *ψ-Ionone in hexane.*
1 ++++ *β-Ionone in hexane.*
2 ——— *Citrylidenecrotonaldehyde in alcohol.*
2 – – – – *Citrylidenecrotonaldehyde in hexane.*
2 ++++ *α-Ionone in alcohol.*

1932, 495, 225), clearly indicating an intensive band in the spectral region of 2200 A.: this is doubtless due to the presence of a conjugated system consisting of the C=N group and the (substituted) amino-group –C=N–NH– (cf. Burawoy, *loc. cit.*; *J. pr. Chem.*, **1932, 135**, 145).

FIG. 4.



1 – – – – – *Citralsemicarbazone-a and -b.*
1 ——— *Citrylideneacetaldehydesemicarbazone in alcohol.*
2 – – – – – *ψ-Iononesemicarbazone.*
2 ——— *α-Citrylidenecrotonaldehydesemicarbazone.*

In the spectra of the semicarbazones of citral-*a* and -*b* (VI, $n = 0$), citrylideneacetaldehyde (VI, $n = 1$), *ψ*-ionone (VII), and citrylidenecrotonaldehyde-*a* (VI, $n = 2$) (cf. Fig. 4), the intensive band of acetonesemicarbazone is displaced to longer wave-lengths with

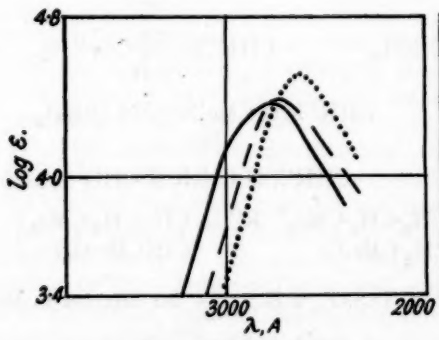
increasing length of the chromophoric conjugated system. The intensity in the case of (VI, $n = 2$) is smaller than those of the other semicarbazones, as was also found for the carbonyl compounds themselves.

	Compound.*	$\lambda_{max.}$, A.	$\epsilon_{max.}$	Remarks.
(i)	Citral	3240	65	From sodium bisulphite derivative
		2380	13,500	
(ii)	† ,,	3360	48	
		2325	14,700	
(iii)	Citrylideneacetaldehyde	2900	15,960	From semicarbazone, m. p. 167°
(iv)	† ,,	2800	15,470	
(v)	Citrylidenecrotonaldehyde	3140	12,490	From semicarbazone, m. p. 160°
(vi)	† ,,	3070	11,550	
(vii)	ψ-Ionone	2910	21,800	From semicarbazone, m. p. 142°
(viii)	† ,,	2820	22,800	
(ix)	β-*cyclo*Citral	3280	43	From semicarbazone, m. p. 167°
		2445	8,300	
(x)	† ,,	3380	38	
		2410	10,100	
(xi)	β-Ionone	2935	8,700	From semicarbazone, m. p. 148°
(xii)	† ,,	2805	7,700	
(xiii)	α-Ionone	2285	14,300	From oxime, m. p. 89°
	Semicarbazone of			
(xiv)	Citral-*a*	2720	31,350	M. p. 164°
(xv)	Citral-*b*	2720	31,350	M. p. 171
(xvi)	Citrylideneacetaldehyde	3045	47,200	M. p. 167
(xvii)	ψ-Ionone	2995	45,400	M. p. 142
(xviii)	Citrylidenecrotonaldehyde-*a*	3255	27,100	M. p. 160
(xix)	β-*cyclo*Citral	2720	23,800	M. p. 167
(xx)	β-Ionone	2765	23,300	M. p. 148
(xxi)	α-Ionone	2635	31,600	M. p. 139
	Phenylsemicarbazone of			
(xxii)	Citrylidenecrotonaldehyde-*a*	3320	28,700	M. p. 134
		2370	19,150	
(xxiii)	Citrylidenecrotonaldehyde-*b*	3320	26,900	M. p. 173
		2365	15,400	
(xxiv)	β-*cyclo*Citral	2805	26,600	
		2365	19,800	
(xxv)	Aldehyde or ketone, $C_{15}H_{22}O$	2765	40,600	M. p. 182—183
		2365	21,100	

* The solvent was alcohol, except for the solutions marked †, for which it was hexane.

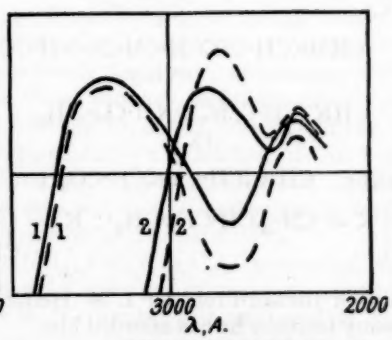
β-*cyclo*Citralsemicarbazone (VIII), like its acyclic isomer, absorbs at 2720 A., but, as with the free carbonyl compounds, the former has a lower intensity (Fig. 5). It is, therefore,

FIG. 5.



..... α-*Ionone*semicarbazone.
– – – – – β-cyclo*Citral*semicarbazone.
——— β-*Ionone*semicarbazone.
All in alcohol.

FIG. 6.



Phenylsemicarbazones of
1 ——— *Citrylidenecrotonaldehyde*-a.
1 – – – – – *Citrylidenecrotonaldehyde*-b.
2 ——— β-cyclo*Citral*.
2 – – – – – *Aldehyde or ketone*, $C_{15}H_{22}O$.
All in alcohol.

surprising that β-ionononesemicarbazone (IX) exhibits a well-defined absorption band at 2765 A. (Fig. 5) instead of in the region of 3000 A. Not only does it absorb at a much

shorter wave-length than ψ-iononesemicarbazone (VII), but comparison with β-*cyclo*citral-semicarbazone (VIII) shows that the introduction of the additional ethenoid linkage has only a very slight effect on the position of the band. This phenomenon is the more remarkable, since the positions of the bands for both β-*cyclo*citral (2445 A.) and β-ionone (2935 A.) are normal. The suggestion that β-iononesemicarbazone does not possess the supposed structure is not justified, for two reasons: (i) Pure β-ionone is readily recovered from it by distillation with steam in the presence of phthalic anhydride (the only way of obtaining pure β-ionone, the commercial products containing only 40—50%); (ii) quantitative microhydrogenation by Jackson and Jones's method (J., 1936, 895) establishes the presence of three double bonds (actually 2·99) as compared with two (actually 2·08) in the case of β-*cyclo*citralsemicarbazone (4·66 mg. of β-iononesemicarbazone in decalin require 1·345 c.c. of hydrogen at 756·5 mm. and 19·7°; 5·38 mg. of β-cyclocitral semicarbazone in acetic acid require 1·290 c.c. of hydrogen at 763·5 mm. and 21·9°). It is probable that this anomaly is due to the effect of the steric hindrance of the methyl group on the light absorption (cf. Ley *et al.*, *Ber.*, 1921, **54**, 364; 1923, **56**, 771).

α-Iononesemicarbazone (X) exhibits a band at 2635 A. (Fig. 5), the intensity of which is of the same order as for the open-chain compounds, ring closure, as in the case of α-ionone itself, apparently having little effect.

The phenylsemicarbazones of β-*cyclo*citral and of both the isomeric citrylidenecrotonaldehydes have also been examined (Fig. 6). The phenyl group displaces the absorption bands to longer wave-lengths (60—80 A.), besides showing an additional band in the shorter ultra-violet; this is due to the chromophoric group $C_6H_5{\cdot}NH{\cdot}CO{\cdot}$, for it also appears in the spectrum of acetanilide.

Heilbron *et al.* (J., 1935, 584) described the preparation of a substance $C_{15}H_{32}O$ by dry distillation of the barium salt of β-ionylideneacetic acid (XI) with barium formate under reduced pressure. This was at first thought to be β-ionylideneacetaldehyde (XII), but examination of its absorption spectrum and of that of its phenylsemicarbazone showed that it could not have this structure, containing three ethenoid linkages in conjugation with a carbonyl group, for the phenylsemicarbazone exhibits a well-defined band at 2765 A. (Fig. 6), indicating that it is derived from an αβ-unsaturated aldehyde or ketone. This discovery was of importance, for the substance is an intermediate in the synthesis of vitamin-*A*.

CRMe:CH·[CH:CH]$_n$·CHO (I.) R'·CHO (II.) CRMe:CH·CH:CH·COMe (III.)

CHR':CH·COMe (IV.) CHR'':CH·COMe (V.) CRMe:CH·[CH:CH]$_n$·CH:N·NH·CO·NH$_2$ (VI.)

CRMe:CH·CH:CH·CMe:N·NH·CO·NH$_2$ (VII.) CHR':N·NH·CO·NH$_2$ (VIII.)

CHR':CH·CMe:N·NH·CO·NH$_2$ (IX.) CHR'':CH·CMe:N·NH·CO·NH$_2$ (X.)

(XI.) CHR':CH·CMe:CH·CO$_2$H CHR':CH·CMe:CH·CHO (XII.)

$$\left[R = CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot};\ R' = \begin{matrix} CH_2{\cdot}CH_2{\cdot}CMe_2 \\ CH_2{\cdot}CMe{:}C{\cdot} \end{matrix};\ R'' = \begin{matrix} CH_2{\cdot}CH_2{\cdot}CMe_2 \\ CH{:}CMe{\cdot}CH{\cdot} \end{matrix}\right]$$

The author thanks Professor I. M. Heilbron, D.S.O., F.R.S., for his interest in this work and the many facilities he has afforded him.

THE UNIVERSITY, MANCHESTER. [*Received, August 14th*, 1940.]

7. *Bunsen's Salt.*

By Harry Irving and G. W. Cherry.

The system NH_4Cl–$(NH_4)_4Fe(CN)_6$–H_2O has been studied at 25° and 40°: the only other solid phase is the double salt $2NH_4Cl,(NH_4)_4Fe(CN)_6$—Bunsen's salt. The existence of the trihydrate described by Hölzl could not be confirmed, and his grounds for formulating this salt as $(NH_4)_6[Fe(CN)_6Cl_2],3H_2O$, with 8-covalent iron, are critically examined. A preliminary note of an *X*-ray study of Bunsen's salt is given, and an explanation is proposed for its alleged chromoisomerides.

The action of ammonium chloride upon Prussian-blue was found by Bunsen (*Pogg. Ann.*, 1835, **36**, 404) to yield fine crystals of a "triple salt" $4NH_4CN,Fe(CN)_2,2NH_4Cl,3H_2O$ [*i.e.*, $2NH_4Cl,(NH_4)_4Fe(CN)_6,3H_2O$] which could be more conveniently prepared from ammonium chloride and ammonium or potassium ferrocyanide. This salt, called Bunsen's salt by subsequent workers, was later prepared by Étard and Bémont (*Compt. rend.*, 1885, **100**, 108), who represented it to be anhydrous although they gave no analyses, and by Freund (*Ber.*, 1888, **21**, 934), by the action on Buff's salt (see below) of alcoholic ammonia. Grailich ("Krystallographisch-optische Untersuchungen," Preisschr., Wien, 1868, 133) studied its optics, and Topsøe (*Arch. Sci. Phys. Nat.*, 1872, **45**, 225) recorded its density as 1·49.

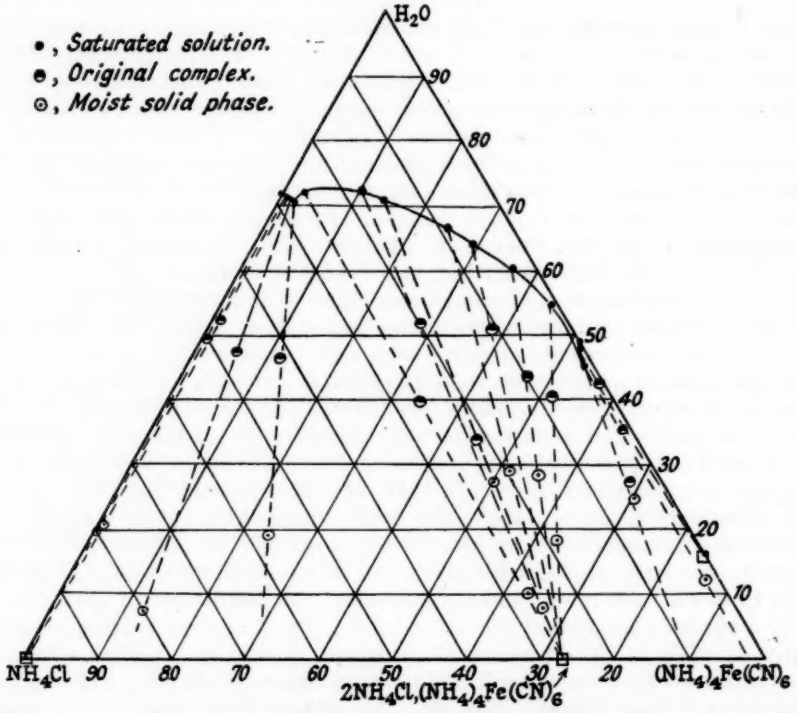
Briggs (J., 1911, **99**, 1027) described two forms of Bunsen's salt: the pale yellow α-form separated from solutions of ammonium chloride and ammonium ferrocyanide containing a little sodium cyanide, whereas the deep amber β-form was obtained from a solution of the two components acidified with dilute acetic acid. The two forms were anhydrous and seemed analytically indistinguishable, yet despite substantially identical solubilities and molecular weights, Briggs formulated them as co-ordination isomers. Both potassium ferrocyanide and ferricyanide were found to give analogous pairs of isomers. When, however, Piutti (*Ber.*, 1912, **45**, 1831) found that the isomer pairs had indistinguishable absorption spectra, and Bennett (J., 1917, **111**, 490) showed that they were crystallographically identical, Briggs (J., 1920, **117**, 1029) suggested that the modified properties of the β-form of potassium ferrocyanide could be explained by assuming that it consisted of the normal, or α-ferrocyanide with about 1% of aquopentacyanide $K_3[Fe(CN)_5(H_2O)]$, *i.e.*, enough to modify the colour and crystal habit, but insufficient to affect the analyses. Presumably a similar explanation was intended for the isomerism of Bunsen's salt.

Recently, in view of the formal analogy which Baeyer and Villiger (*Ber.*, 1902, **35**, 1202) remarked between Bunsen's salt and the oxonium salts $(ROH_2)_4,Fe(CN)_6,2(ROH_2)Cl$ which Buff (*Ann. Chem. Pharm.*, 1854, **91**, 253) obtained by passing hydrogen chloride into an alcoholic solution of hydroferrocyanic acid, Hölzl (*Sitzungsber. Akad. Wien*, 1928, **137**, II*b*, 1110) suggested that these two "double salts" ought to be formulated as $(NH_4)_6[Fe(CN)_6Cl_2]$ and $(ROH_2)_6[Fe(CN)_6Cl_2]$ respectively, both salts containing the same complex anion, admittedly of low stability since their aqueous solutions gave only the analytical reactions of Cl^- and $[Fe(CN)_6]^{4-}$. Subsequently, Hölzl and Stockmair (*ibid.*, 1932, **141**, II*b*, 763) adduced physicochemical evidence for the existence of this complex ion $[Fe(CN)_6Cl_2]^{6-}$ with iron in 8-fold co-ordination. This unorthodox hypothesis, together with the fact that Hölzl's analysis of Bunsen's salt corresponds exactly with that of a trihydrate, induced us to re-examine its composition and constitution.

The phase-rule study of the system NH_4Cl–$(NH_4)_4Fe(CN)_6$–H_2O presented several problems owing to the photosensitivity and ease of oxidation of aqueous solutions of ammonium ferrocyanide, and difficulties inherent in the analysis of mixtures of chloride and ferrocyanide, especially when their molecular proportions are widely dissimilar. Furthermore, the high solubilities of the two salts caused rather viscous solutions which impeded filtration and hindered the isolation of a solid phase even reasonably free from mother-liquor for the "residue method." Known weights of the two salts and air-free water were, therefore, sealed off in a nitrogen atmosphere in glass tubes with specially thin bottoms and brought to equilibrium by shaking in a light-tight zinc box immersed in a thermostat. The phases were separated by filtration through sintered glass in an apparatus immersed in the thermostat, weighed, and analysed volumetrically (see p. 29).

The composition of the original complex being known, analysis of either the resulting saturated solution or the (moist) solid phase would suffice for extrapolation to the composition of the pure solid phase: in many cases both were analysed, and the reliability of a determination could be assessed from the collinearity of the plot of the three sets of concentration data.

The isothermal for 25·1° ± 0·1° is shown in the figure: a substantially similar diagram was obtained at 40·05° ± 0·1°, and throughout this range Bunsen's salt comprises the only new solid phase. A few less accurate measurements at 0° failed to indicate any change in the general character of the phase diagram.



The solid phase appears to be anhydrous $2NH_4Cl,(NH_4)_4Fe(CN)_6$, the solution containing 38·9, 49·7, and 53·4 g. per 100 g. of water at 0°, 25·1°, and 40·05° respectively. Its composition is supported by analyses of the salt prepared in the present work, and of (new) preparations of the α- and β-forms according to Briggs (*loc. cit.*). Data for a preparation from potassium ferrocyanide (Bunsen, *loc. cit.*) and Hölzl's figures are included.

	K, %.	NH_3, %, (a).	Fe, %, (b).	$Fe(CN)_6''''$, %, (c).	Cl, %, (d).
Present authors	0·0	25·8, 25·6	14·2, 14·3	54·2, 54·2	18·2, 18·4
Briggs's α-form	0·0	25·6, 25·8	14·2, 14·25	54·0	18·0
,, β-form	0·0	26·1, 25·8	14·6, 14·4	54·2	18·4
Bunsen's prepn.	4·6	23·5, 23·8	14·0, 14·0	53·7	18·0
Hölzl's ,, ...	0·0	22·9	12·8	—	16·0
Calc. for $2NH_4Cl,(NH_4)_4Fe(CN)_6$	0·0	26·1	14·3	54·2	18·1
,, ,$\frac{1}{2}H_2O$...	0·0	25·4	13·95	53·0	17·7
,, ,$3H_2O$...	0·0	23·0	12·55	—	15·9

(a) Ammonia liberated by alkali. (b) Separated as $Fe(OH)_3$ after ignition with H_2SO_4. (c) Determined by means of ceric sulphate. (d) Determined by Volhard's method.

There is thus no confirmation of Hölzl's trihydrate, which he states was prepared "by Bunsen's method" and "crystallised from water"; unfortunately, the references he quotes are to abstracts of Étard and Bémont's papers (themselves devoid of experimental details), and not to Bunsen's own work.

In preparing Briggs's β-form some Prussian-blue is formed and must be separated by

filtration; much more results during Bunsen's method of preparation from potassium ferrocyanide—which also gives a deep amber product. These observations suggested that the " isomerism " of the β-form might be due, not to admixed ammonium aquopentacyanoferroate (see p. 25), but rather to adsorbed or entrained Prussian-blue. Crystallisation of the pale yellow α-form from a colloidal solution of Prussian-blue in air-free water did, in fact, yield amber, almost brown crystals characteristic of the β-form. Unless absolutely dry, all crystals of the β-form turn green on keeping, whereas the α-form can be preserved unchanged. A similar explanation of the " isomerism " of potassium ferricyanide (Locke and Edwards, *Amer. Chem. J.*, 1898, **21**, 193) has been confirmed by Hauser and Biesalski (*Ber.*, 1912, **45**, 3516), who showed that even 0·001 mol. of Prussian-blue per mol. of ferricyanide would modify its colour.

Hölzl's grounds for formulating Bunsen's salt as $(NH_4)_6[Fe(CN)_6Cl_2]$ with 8-co-ordinated iron are derived from conductivity and transport measurements. Although the conductivity in water at 25° of mixtures of ammonium chloride and ammonium ferrocyanide in various proportions was a linear function of their molar fraction in 0·01M-solution, yet Hölzl and Stockmair (*loc. cit.*) found that the conductivities of 0·02, 0·05, and 0·10M-mixtures were invariably less than those calculated by this linear relationship, the defect increasing with increasing concentration. They interpreted these results (some of which, recalculated as equivalent conductances, are reproduced below) as evidence for the formation of " one or more compounds " with the original ions recombined " to higher complexes of lower mobility " : the gradual disappearance of the conductivity defect was taken as evidence for the displacement of the equilibrium $[Fe(CN)_6Cl_2]^{6-} \rightleftharpoons 2Cl^- + [Fe(CN)_6]^{4-}$ to the right with increasing dilution.

Molar ratio $\frac{(NH_4)_4Fe(CN)_6}{NH_4Cl}$	0·1M.			0·02M.		
	$\Lambda^{25°}_{calc.}$	$\Lambda^{25°}_{obs.}$	Defect.	$\Lambda^{25°}_{calc.}$	$\Lambda^{25°}_{obs.}$	Defect.
10 : 0	312	312	—	405	405	—
9 : 1	295	249	46	385	345	38
8 : 2	278	233	45	360	325	35
7 : 3	261	221	40	338	305	33
6 : 4	244	203	41	315	295	20
5 : 5	228	190	38	293	280	13
4 : 6	211	178	33	270	265	5
3 : 7	194	167	17	255	248	7
2 : 8	177	161	10	230	225	5
1 : 9	160	151	9	203	200	3
0 : 10	143	143	—	180	180	—

Now such conductivity defects are, in point of fact, predicted by theory and realised experimentally even where complex-ion formation can scarcely be involved (*e.g.*, in mixtures of alkali halides, Van Rysselberghe and Nutting, *J. Amer. Chem. Soc.*, 1937, **59**, 333); yet there have been many cases (cf. Van Rysselberghe, Grinnell, and Carlson, *ibid.*, p. 336) where the magnitude of the conductivity defects has led investigators incorrectly to postulate complex-ion formation for, as Davies has pointed out (J., 1938, 448), the conductivity of a mixture of two electrolytes of the same equivalent concentration will differ from that calculated by an additive formula on account of two factors, (*a*) the change in mobility of the ions, and (*b*) the change in ionic concentration when dissociation is incomplete. For example, the deviations which in mixtures of magnesium chloride (completely dissociated) and sodium sulphate amount to as much as 10% of the total conductivity are due to the formation of magnesium sulphate ion-pairs (Davies, *loc. cit.*). Now while 0·1M-ammonium chloride is 87% dissociated, 0·1M-potassium ferrocyanide is only about 50% dissociated, and in view of the substantially identical mobilities of K^+ and NH_4^+ we may take the same figure for 0·1M-ammonium ferrocyanide: the corresponding figures for 0·01M-solutions are 97% and 73%. The " common-ion " effect of adding highly dissociated ammonium chloride to poorly dissociated ammonium ferrocyanide will be still further to reduce the dissociation of the latter and the conductivity of the mixture will fall. On the other hand, addition of ammonium ferrocyanide to ammonium chloride solutions should produce a less significant conductivity decrease. Hölzl's data illustrate both these predictions, and the maximum conductivity defect occurs with less than 10 mols.% of ammonium chloride and then decreases with increasing ferrocyanide content. On the

other hand, were the complex $[Fe(CN)_6Cl_2]^{6-}$ to be formed, the maximum defect would occur at the corresponding composition, *i.e.*, about 66 mols.% of ammonium chloride. The gradual appearance of a green colour and increase in the conductivity of ammonium chloride–ferrocyanide mixtures over a period of some 18 hours is not due, as Hölzl inferred, to any decomposition of the hypothecated anion $[Fe(CN)_6Cl_2]^{6-}$, but is an oxidation and photo-change which can be arrested indefinitely in the absence of air and light.

Finally, Hölzl and Stockmair (*loc. cit.*) record a single transport experiment in which the passage of electricity (quantity not given) through a 0·1M-solution of Bunsen's salt caused migration of chloride and ferrocyanide ions in the molecular ratio 2 : 1·03. Since the ionic mobilities are 76·6 and 100·8 respectively, this experiment appears to afford weighty evidence for the real existence of the complex anion $[Fe(CN)_6Cl_2]^{6-}$. We could not, however, confirm this unique experiment, for under all conditions oxidation of ferro- to ferri-cyanide took place. Hölzl did not consider this contingency, and the analytical method which he employed to determine the change in halogen content in the anode compartment (difference between estimate of total $[Fe(CN)_6]^{4-} + [Cl^-]$ by Volhard, and $[Fe(CN)_6]^{4-}$ iodometrically or manganometrically) leads to fictitious high values for $[Cl^-]$ since the argentimetric titre is increased by any ferricyanide formed, whilst oxidation simultaneously decreases $[Fe(CN)_6]^{4-}$. Our experiments showed that oxidation was indeed the principal reaction, and that the concentration of chlorine in the anode compartment, far from increasing as Hölzl recorded, did in fact decrease slightly although chlorate ions could not be detected qualitatively.

A number of experiments on the freezing point of mixtures of calcium ferrocyanide and calcium or barium chloride likewise failed to produce evidence in favour of complex-ion formation of the type postulated by Hölzl.

Isomorphous with Bunsen's salt is the bromine analogue (Bunsen and Himly, *Pogg. Ann.*, 1836, **38**, 208): we have repeated its preparation and confirm the formula as anhydrous $2NH_4Br,(NH_4)_4Fe(CN)_6$. Attempts to prepare double salts from ammonium ferrocyanide and ammonium cyanide, fluoride, or iodide were unsuccessful, and no analogue of Bunsen's salt from potassium ferrocyanide and chloride could be obtained although Étard and Bémont (*loc. cit.*) claim to have prepared $2NH_4Cl,K(NH_4)_3Fe(CN)_6$ and $2NH_4Cl,(NH_4)KH_2Fe(CN)_6$ from potassium ferrocyanide and ammonium chloride. Although Denigés (*Bull. Soc. chim.*, 1916, **19**, 86) has proposed "structural" formulæ for Bunsen's salt and the latter compounds, they are nowadays of no significance and further progress can best be made through a detailed *X*-ray analysis. The preliminary work (below) confirms our formulation and negatives the existence, even in the crystalline state, of the complex anion hypothecated by Hölzl.

X-Ray Analysis.—Messrs. G. W. R. Bartindale and H. M. Powell report as follows: The results of the goniometric and optical examination of the crystals agree closely with those of Bennett (*loc. cit.*), except that an additional form {111} was observed. *X*-Ray examination gave for the hexagonal unit cell $a_0 = 9{\cdot}24$, $c_0 = 18{\cdot}92$ A., and $c : a = 2{\cdot}046$; goniometrically $2c : a = 2{\cdot}038$. The density, by flotation, is 1·40 g./c.c., and there are 3 molecules per unit cell. The calculated cell molecular weight agrees closely with the theoretical value and is incompatible with the presence of water of crystallisation. The absent spectra are those characteristic of a rhombohedral lattice. No evidence of the absence of a symmetry centre could be obtained, and the space group is probably $R\bar{3}$.

Referred to the hexagonal cell, iron atoms lie at (000), and chlorine atoms at $(00\overset{\pm}{z})$, and at the equivalent points. Preliminary structure determination shows that $z \approx \frac{1}{6}$. This means that the Fe–Cl distance is about 6 A., and at once excludes any possibility of a covalent link between these atoms. A detailed structure determination is in progress.

Experimental.

Materials.—Ammonium ferrocyanide was prepared from "AnalaR" potassium ferrocyanide through the hydroferrocyanic acid–ether complex (Mittasch and Kuss, *Z. Elektrochem.*, 1928, **34**, 159), the latter being freed from potassium and hydrogen chlorides by repeated washing (Wagener and Tollens, *Ber.*, 1906, **39**, 410). The preparation was carried out in a room illuminated by red light, and the product was preserved in a vacuum over calcium chloride.

Qualitative tests (Feigl, "Qualitative Analyse mit Hilfe von Tupfelreaktionen," 2nd Edition, pp. 267, 276) proved the absence of potassium and chloride. The salt precipitated from aqueous solution by alcohol retained about 1½ mols. of water, which could only be removed with difficulty and some decomposition. Analyses of typical preparations established its composition and purity.

	(1).	(2).	(3).	(4).	(5).	(6).	(7).
$[Fe(CN)_6]^{4-}$, %	68·5	69·0	68·4	72·9	72·5	74·6	68·2
$(NH_4)^+$, %	23·35	23·3	23·8	24·6	24·7	25·4	23·2
H_2O, % (by diff.)	8·1	7·65	8·5	2·5	2·8	0·0	8·6
Ratio $\frac{[Fe(CN)_6]^{4-}\%}{(NH_4)^+\%}$ ...	2·93	2·97	2·88	2·97	2·94	2·94	2·94

(1) Original preparation. (2) After 1 week in a vacuum. (3) Preparation dissolved in ice-water and reprecipitated. (4) Benzene added to salt and distilled off rapidly. (5) Benzene added and distilled off below 90°. (6) Calc. for $(NH_4)_4Fe(CN)_6$. (7) Calc. for $(NH_4)_4Fe(CN)_6.1\frac{1}{2}H_2O$.

Each preparation of ammonium ferrocyanide was analysed before use and was employed with "AnalaR" ammonium chloride in making up complexes by weight as described above (p. 25). Preliminary experiments showed that in the absence of light and oxygen the decomposition of N/10-ammonium ferrocyanide solutions did not exceed 0·3% in 10, and 1% in 30 days at 25°. Though equilibrium was reached within 48 hours, each complex was shaken in a thermostat regulated to ± 0·05° for at least 4 days before analysis.

Analysis.—Samples of the phases were diluted with air-free water to convenient known volumes. Ferrocyanide was determined with N/20-ceric sulphate standardised against anhydrous "AnalaR" potassium ferrocyanide (de Beer and Hjort, *Ind. Eng. Chem., Anal.,*

System NH_4Cl–$(NH_4)_4Fe(CN)_6$–H_2O.

[A = NH_4Cl; B = $2NH_4Cl,(NH_4)_4Fe(CN)_6$; F = $(NH_4)_4Fe(CN)_6$.]

Solution.			Original complex.			Moist solid.			Solid phase.
A, %.	F, %.	H_2O, %.	A, %.	F, %.	H_2O, %.	A, %.	F, %.	H_2O, %.	
				At 0·0°.					
13·6	9·7	76·7	15·5	15·8	68·7	24·0	56·0	20·0	B
8·7	18·9	72·4	10·3	22·1	67·6	—	—	—	B
7·0	21·9	71·1	16·5	49·1	34·4	20·4	59·6	20·0	B
				At 25·1°.					
28·3	0·0	71·7		A + H_2O		—	—	—	A
28·0	0·3	71·7	50·1	0·1	49·8	80·1	0·05	19·8	A
27·8	0·4	71·8	46·6	0·2	53·2	79·4	0·2	20·4	A
27·3	1·2	71·5	41·8	10·6	47·6	56·9	23·8	19·3	A, B
27·3	1·0	71·7	47·3	4·9	47·8	80·0	12·8	7·2	A, B
25·3	2·3	72·4	26·1	33·9	40·0	26·0	63·5	10·5	B
17·1	10·3	72·6	20·0	28·0	52·0	25·7	66·4	7·9	B
14·7	14·0	71·3	21·6	44·6	33·8	22·6	50·0	27·4	B
8·5	24·7	66·8		B + H_2O		19·2	51·5	29·3	B
6·2	30·0	63·8	10·6	38·3	51·1	—	—	—	B
3·7	36·7	59·6	9·7	46·6	43·7	16·0	55·7	28·3	B
0·8	44·6	54·6	7·6	51·8	40·6	18·2	63·0	18·8	B
0·6	53·8	45·6	4·0	68·4	27·6	4·7	70·3	25·0	B, F
1·0	53·6	45·5	0·5	63·9	35·6	0·8	87·1	12·1	B, F
0·3	51·7	48·0	0·5	56·8	42·7	0·05	64·9	35·1	F
0·0	51·3	48·7		F + H_2O		—	—	—	F
				At 40·05°.					
31·6	—	68·4		A + H_2O		—	—	—	A
29·9	0·8	69·3	50·1	0·5	49·4	—	—	—	A
29·6	1·3	69·1	49·4	1·0	49·6	—	—	—	A
28·4	1·8	69·8	49·3	10·5	40·2	—	—	—	A, B
28·4	1·6	70·0	29·4	30·7	39·9	—	—	—	A, B
24·3	4·5	71·2	25·0	20·5	54·5	26·7	60·0	13·3	B
23·6	5·2	71·2	24·9	25·1	50·0	—	—	—	B
15·9	13·9	70·2	19·7	29·9	50·4	—	—	—	B
9·5	25·2	65·3		B + H_2O		25·0	67·2	7·8	B
3·7	41·2	55·1	9·4	48·2	42·4	—	—	—	B
1·0	54·6	44·4	5·1	65·1	29·8	—	—	—	B, F
1·1	53·3	45·0	10·0	59·7	30·3	—	—	—	B, F
1·0	54·6	44·4	5·1	65·1	29·8	—	—	—	F
0·6	54·1	45·3	1·0	60·4	38·6	—	—	—	F
0·9	54·9	44·2	0·6	61·9	37·5	0·6	74·1	25·3	F
0·0	54·7	45·3		F + H_2O		—	—	—	F

1935, **7**, 120), *N*-phenylanthranilic acid being used as internal indicator (Syrokomsky and Stiepin, *J. Amer. Chem. Soc.*, 1936, **58**, 928). Silver chloride and ferrocyanide were then precipitated together by a small known excess of N/10-silver nitrate, the excess being determined by the Volhard method. The concentration of chloride ion is then obtained by subtracting four times the cerimetric titre from this argentimetric value. Since this method would clearly prove unreliable for mixtures with small proportions of ammonium chloride, an alternative procedure was adopted wherein ferrocyanide ion was quantitatively precipitated as zinc ammonium ferrocyanide (Cone and Cady, *J. Amer. Chem. Soc.*, 1927, **49**, 356) and removed before the determination of the halogen. Control experiments showed that this process could be used for mixtures containing as little as 1% of ammonium chloride.

Transport Experiments.—These were carried out in a conventional apparatus in series with a silver coulometer. In a preliminary experiment in which a silver anode was employed, the passage of 162·7 coulombs through a M/10-aqueous solution of Bunsen's salt appeared to cause an increase of 0·0150 g.-mol./l. in the concentration of ammonium chloride and a decrease of 0·0074 g.-mol./l. in that of ammonium ferrocyanide. These results were worthless, for qualitative tests (Feigl, *op. cit.*, p. 300) showed the presence of ferricyanide ions. In subsequent experiments a platinum anode and cathode were used, and chloride and ferrocyanide having been determined as above (p. 29), ferricyanide was determined iodometrically in an aliquot portion of the anode solution, the excess of ferrocyanide and that formed during the titration being precipitated as $K_2Zn_3[Fe(CN)_6]_2$ by addition of zinc sulphate (Vogel, " Quantitative Inorganic Analysis," 1939, p. 435). The results of three experiments were :

a.	b.	c.	d.	e.	f.	g.	h.	i.	j.
0·2057	0·2004	0·1164	0·0937	0·0299	0·1236	+0·0072	0·0053	89·0	97·2
0·2190	0·2143	0·1249	0·1007	0·0311	0·1318	+0·0069	0·0047	70·0	102
0·1969	0·1959	0·0998	0·0786	0·0205	0·0991	−0·0007	0·0010	50·9	96·2

a, b = initial and final $[NH_4Cl]$; c, d = initial and final $[(NH_4)_4Fe(CN)_6]$; e = increase in $[(NH_4)_3Fe(CN)_6]$—initially zero; f = $[(NH_4)_4Fe(CN)_6]$ had no oxidation taken place; g = the increase in $[(NH_4)_4Fe(CN)_6]$ in the absence of oxidation; h = *decrease* in $[NH_4Cl]$; i = number of coulombs passed; j = the current efficiency (*q.v.*).

It is obvious that the preponderating change is the electrolytic oxidation of ferro- to ferricyanide which proceeds with approximately theoretical efficiency. The changes in $[NH_4Cl]$ (h), and in $[(NH_4)_3Fe(CN)_6 + (NH_4)_4Fe(CN)_6]$ (f), fall within the limits of accuracy of the experiments.

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8. *A Study of the Photolysis of Organic Nitrogen Compounds. Part III. Methyl* iso*Cyanate.*

By DAPHNE A. BAMFORD and C. H. BAMFORD.

The absorption spectra, and the mercury-sensitised and the direct photolysis of gaseous methyl *iso*cyanate in the near ultra-violet have been studied. The products of decomposition can be accounted for in both cases by the simultaneous occurrence of two primary acts, producing NCO and CH_3N radicals severally. The relative importance of these processes depends on the temperature. The mechanism of sensitisation is briefly discussed. By irradiation in the presence of nitric oxide it is shown that both the above radicals enter into simple and nearly quantitative reactions with this gas.

CONTINUING the study of the formation and reactions of free radicals containing nitrogen, we have investigated the photodecomposition of methyl *iso*cyanate. The absorption spectrum of this substance (slightly contaminated with sulphur dioxide) was studied by Woo and Liu (*J. Chem. Physics*, 1935, **3**, 544; 1937, **5**, 499), who recorded the absence of structure in the spectrum, and, using the pure ester, we confirm their results. Hence, the primary act in the photolysis is most probably a dissociation into radicals. The results now described are consistent with the view that this dissociation is twofold :

$$CH_3{\cdot}NCO + h\nu \begin{cases} \nearrow CH_3 + NCO & \ldots\ldots\ldots (1) \\ \searrow CH_3N + CO & \ldots\ldots\ldots (2) \end{cases}$$

The mercury-sensitised decomposition has been studied in detail. The NCO radicals under these conditions appear to interact to form nitrogen and carbon monoxide, whereas the CH_3N radicals react with methyl *iso*cyanate in the cold to form a white cloud. At higher temperatures no cloud is formed, but instead a viscous oil appears, which may be a polymer of CH_3N. The direct photolysis is similar, except for the fact that practically all the NCO radicals seem to be hydrogenated to HCNO. An explanation of this is suggested later. Both the NCO and the CH_3N enter into simple reactions with nitric oxide, and these may be used both as a check upon the mechanism of photolysis suggested, and as a test for the presence of these radicals in other reactions.

Experimental.

1. *Preparation of Materials.*—Methyl *iso*cyanate, prepared from methyl sulphate and potassium cyanate (Slotta and Lorenz, *Ber.*, 1925, **58**, 1320), was fractionated, and the product of b. p. 44° was further fractionated in a vacuum. A few units % of sulphur dioxide always remained after this treatment, but this could be removed completely by passing the vapour over anhydrous sodium carbonate, followed by a further fractionation at — 80° to remove the carbon dioxide formed. The absorption spectrum of the final product showed no trace of the characteristic sulphur dioxide bands. It was necessary to keep the substance at — 80° to prevent polymerisation.

2. *Apparatus.*—A Hilger E3 spectrograph was used for photographing the absorption spectrum. The source of light was a hydrogen lamp, and a quartz absorption tube 1 m. long was employed. This could be heated electrically to any desired temperature.

The apparatus used for the photolysis was similar to that already described (Bamford, *Trans. Faraday Soc.*, 1939, **35**, 568). The quartz reaction vessel was, however, arranged inside a furnace so that photolysis could be carried out at elevated temperatures. The gaseous products were removed for analysis in two fractions at — 190° and — 80° severally. For studying the sensitised reaction, a mercury lamp with water-cooled electrodes consuming 200 watts and emitting 90% resonance radiation was used. The direct photolysis was carried out by means of a 250-watt mercury arc running hot.

3. *Results.*—The absorption spectrum appears to be completely continuous. At 15° the highest pressure used was 50 mm. and the long-wave limit of the absorption band was approximately 2350 A. No appreciable change occurred when the temperature was raised to 140°. With a pressure of 70 mm. at this temperature the long-wave limit of the band was 2400 A. The absorption extends to the short-wave limit of the plate. The effective wave-lengths in the experiments described below, in which the hot arc was used, thus lay between 2400 and 2100 A., since the lamp gave only very feeble lines below 2100 A. Similarly, with the cold arc the reaction was sensitised at least to the extent of 90%.

The gaseous products for the sensitised reaction are shown in Table I. The results are scaled to $N_2 = 100$ to facilitate comparison. The figure in parentheses for N_2 is the volume of nitrogen (in c.c. at N.T.P.) obtained in the experiment. No special precautions were taken to ensure the same intensity in each experiment.

Table I.

Temp.	Time of irradn. (mins.).	Initl. press. of CH_3·NCO (mm.).	Products, CO.	N_2.	CH_4.	C_2H_6.	H_2.	Ratio of primary acts (2)/(1).
20°	50	150	350	100 (1·64)	30	83	0	0·75
20	20	106	350	100 (0·46)	28	82	19	0·66
20	52	46	355	100 (0·60)	39	80	3	0·76
139	26	129	394	100 (0·18)	65	65	9	0·93
160	25	120	477	100 (0·18)	67	66	37	1·20
234	14½	148	547	100 (0·17)	100	48	61·5	1·43
247	25	131	565	100 (0·20)	165·5	19	55	1·55
307	9	159	670	100 (0·14)	220	0	60	2·05
307	20	166	635	100 (0·28)	227	0	40	1·98
307	50	162	715	100 (0·40)	220	0	120	1·98
347	12	140·5	811	100 (0·13)	222	0	122	2·45

The results indicate that the methane and ethane originate from methyl radicals. At the lower temperatures the majority of these form ethane, but as the temperature is raised an increasingly large proportion becomes hydrogented to methane. The yield of methane with respect to ethane increases rapidly between 230° and 260°; above the latter temperature no

ethane is formed. Over the whole range of temperature the total methyl is practically equivalent to the nitrogen, *i.e.*, $CH_4 + 2C_2H_6 = 2N_2$. This would be the case if the primary act was the dissociation (1) followed by the reaction

$$2NCO \longrightarrow N_2 + 2CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The yield of carbon monoxide is considerably greater than can be accounted for by these reactions. This is best explained by the occurrence of the second primary act (2).

It will be noticed that considerable amounts of hydrogen can be produced, especially at the higher temperatures. The yields of hydrogen vary markedly with the period of irradiation and also the rate of reaction, and it therefore seems clear that the hydrogen arises from a secondary photolysis. From the experimental results, especially those at 307°, it is seen that the production of hydrogen is accompanied by the formation of a roughly equivalent volume of carbon monoxide. This suggests that the source of these compounds is formaldehyde. To test this, a short irradiation was carried out at 307°, and the reaction vessel was removed after being allowed to cool. On shaking the contents with water and applying Schryver's test a strong positive result was obtained. A blank test, carried out under similar conditions but without irradiation, was negative.

After a prolonged irradiation at high temperatures during which most of the *iso*cyanate was decomposed, hydrogen cyanide in considerable quantities could be detected among the products. At ordinary temperatures this forms a solid addition compound with the ester and so may escape detection. At high temperatures the compound dissociates (cf. Slotta and Tschesche, *Ber.*, 1927, **60**, 1022), but in order to detect the hydrogen cyanide sufficient methyl *iso*cyanate must be decomposed to give an excess of the former over any undecomposed ester. The presence of formaldehyde and hydrogen cyanide makes it difficult to observe directly the amount of the ester decomposed, since they cannot readily be separated from the unchanged ester.

In order to obtain additional evidence for the two primary acts (1) and (2), the sensitised decomposition was carried out in the presence of nitric oxide. This was done at two temperatures, the results being given in Table II.

TABLE II.

Temp.	Initl. $CH_3 \cdot NCO$ (c.c.).	Initl. NO (c.c.).	Products (c.c.). CO.	N_2.	CO_2.	N_2O.	NO used (c.c.).	Ratio of primary acts (2)/(1).
20°	11·5	6·2	1·5	1·2	1·1	1·4	5·5	0·79
307	5·1	3·1	1·26	0·56	0·5	1·1	3·0	2·2

The mercury-sensitised decomposition of nitric oxide has been shown by Noyes (*J. Amer. Chem. Soc.*, 1931, **53**, 514) to be very slow. To confirm this in the present conditions, 63 mm. of nitric oxide were irradiated for one hour. Less than 0·1 c.c. of nitrogen was produced, and it may be concluded therefore that the substances given in Table II are produced almost completely by interaction of nitric oxide and the products of photolysis of the *iso*cyanate. The results are accounted for by the reactions:

$$NCO + NO \longrightarrow N_2 + CO_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$
$$CH_3N + NO \longrightarrow CH_3 + N_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

It will be noticed that at both temperatures the nitrogen and carbon dioxide are approximately equivalent. The methyl radicals formed in (5) and in the primary act (1) also interact with nitric oxide, mainly according to the equation:

$$CH_3 + NO \longrightarrow H_2O + HCN \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

(see, *e.g.*, Bamford, J., 1939, 17). The possibility of the production of carbon dioxide by reaction between water formed in (6) and methyl *iso*cyanate was also investigated. 15 Mm. of water vapour were mixed with 100 mm. of methyl *iso*cyanate in the reaction vessel and allowed to stand for one hour. There was no change in pressure at the end of this time and less than 0·1 c.c. of carbon dioxide had been formed. Reaction (4) is thus considered to be the only source of carbon dioxide. The absence of hydrocarbon products in these experiments is further evidence that these substances are produced from methyl radicals. The volume of nitric oxide used, observed experimentally, agrees well with that to be expected on the basis of equations (4), (5), and (6), as may be deduced from Table II.

From the ratios of the probabilities of the primary acts (1) and (2) in Table I, it will be noticed that (2) becomes increasingly important as the temperature is raised. The experiments with

nitric oxide also enable the ratio to be estimated, and the results at the two temperatures employed agree well with those in Table I. This affords some confirmation for the suggested primary acts, and also for the reactions (4) and (5).

An approximate estimation of the quantum yield for the sensitised reaction at 307° was made by a comparison of the rate of photolysis with that of acetone vapour under similar conditions. It is necessary to assume that the rate of absorption of energy is the same in both cases. This is probably nearly true, since the mercury vapour present would absorb practically all the resonance light emitted. Further, it may be taken that the quantum yield of carbon monoxide in the sensitised decomposition of acetone vapour at 307° is not very different from that in the direct reaction, *i.e.*, unity (Leermakers, *J. Amer. Chem. Soc.*, 1934, **56**, 1899). Hence the absorption of resonance radiation by the acetone vapour will not invalidate the calculation. Pressures of 50 mm. of methyl *iso*cyanate and acetone vapour were used, and irradiation continued for 10 minutes. The mean volumes of carbon monoxide evolved (two experiments) were: from methyl *iso*cyanate, 0·92 c.c.; from acetone, 0·90 c.c. Hence the quantum yield of carbon monoxide from methyl *iso*cyanate is approximately unity at 307°. This is consistent with the mechanism of equations (1), (2), and (3), according to which the maximum value of the quantum yield is unity. The determination of the quantum yield at lower temperatures presents difficulties, since the formation of the cloud interferes with the estimation of the light absorption.

The results of a number of experiments with the hot arc are given in Table III. These results differ from those obtained with the sensitised reaction in two particulars: there is

TABLE III.

Temp.	Time, mins.	Initl. $CH_3{\cdot}NCO$ (mm.).	Products (c.c. × 10^3, N.T.P.). CO.	N_2.	CH_4.	C_2H_4.	H_2.	Ratio of primary acts (2)/(1).
25°	123	*ca.* 95	90	4	22	37	10·5	0·82
150	60	,,	140	0·5	28·9	31·5	30	1·18
300	41	,,	155	3	57	0	31	2·1
310	30	,,	154	3	55	0	39	2·0
330	18	,,	150	7	47	0	37	2·2
370	30	,,	209	5	50	0	56	2·6
395	19	,,	174	0	39·5	0	63	2·8
420	18	,,	164	4	30	0	55	3·4
15	540	114	115	9	16	51	10	0·74

generally more hydrogen, and considerably less nitrogen, formed in the present experiments. The former can readily be accounted for, since formaldehyde absorbs strongly between 2500 and 3100 A., while methyl *iso*cyanate is practically transparent in this region. The hot arc emits a number of strong lines between these wave-lengths, and the formaldehyde would thus undergo considerable photolysis. In the case of the cold arc the decomposition would be mainly sensitised, and since the aldehyde would only be formed in low pressures for short periods of irradiation, the secondary decomposition would be considerably less.

From the low yield of nitrogen it may be concluded that the NCO radicals in these circumstances enter into other reactions, rather than (3): the most probable of these would seem to be hydrogenation at the expense of the methyl *iso*cyanate, with formation of cyanic acid, which would polymerise and escape photolysis. At the end of an experiment the cloud had settled as a deliquescent solid on the walls of the vessel, and on treatment with a little water it evolved ammonia. This behaviour suggests the presence of cyanic acid. No ammonia was evolved when the cloud produced in the sensitised reaction was treated similarly.

DISCUSSION.

The preceding results have been shown to be in agreement with the view that photolysis of methyl *iso*cyanate results in the primary formation of two radicals containing nitrogen. The univalent NCO decomposes bimolecularly or hydrogenates, while the bivalent CH_3N appears to be less reactive and only enters into polymerisation reactions unless NO is present. This agrees with previous results, which have pointed to the tendency of other bivalent radicals, *e.g.*, $CH_3{\cdot}N{:}CH_2$, produced from nitrosoamines and amines, to polymerise, probably after rearrangement (Bamford, J., 1939, 12).

The primary act (1) is endothermic to the extent of about 49 kg.-cals. (taken from Pauling, "The Nature of the Chemical Bond," 1939), which is much smaller than the

minimum quantum absorbed (*ca.* 112 kg.-cals. for the 2536 A. line). Woo and Liu (*loc. cit.*) have concluded that this is the only decomposition which is energetically possible. The latest value for the C—N link (94 kg.-cals.) suggests that this is not the case; also allowance must be made for the excitation energy of the carbonyl group, which is liberated in passing to the non-valent state (in carbon monoxide). If the latter energy is taken as 69 kg.-cals. (cf. Norrish, *Trans. Faraday Soc.*, 1934, **30**, 103),* the primary act (2) is seen to be about 25 kg.-cals. endothermic.

As mentioned previously, reaction (3) is much more important in the sensitised than in the direct photolysis. In order to account for this apparent inconsistency in the behaviour of the NCO radical it may be suggested that the process of sensitisation leading to the decomposition (1) is not merely the transfer of energy from the excited mercury atom to the methyl *iso*cyanate molecule, but rather the reaction

$$Hg^* + CH_3{\cdot}NCO \longrightarrow [HgNCO] + CH_3 \quad . \quad . \quad . \quad . \quad . \quad (7)$$

It is conceivable that HgNCO, probably existing as a radical, would not hydrogenate so readily as NCO, but would react according to (3). In the direct reaction HgNCO is not formed and (3) is much less important, since most of the radicals are hydrogenated. It can be seen by comparing Tables I and II that this hydrogenation of the NCO radicals on methyl *iso*cyanate is not accompanied by the formation of carbon monoxide: also from Table I it is clear that no carbon monoxide results from the formation of methane by the reaction between methyl radicals and methyl *iso*cyanate (compare, *e.g.*, the results for 234° and 247°). The CH_2NCO residue from the *iso*cyanate presumably polymerises.

The secondary formation of hydrogen occurs more readily at the high temperatures (Table I), suggesting an increased formation of formaldehyde under these conditions, a plausible reaction being

$$CH_3N + CH_3{\cdot}NCO \longrightarrow (CH_3N,HCN) + H_2CO \quad . \quad . \quad . \quad . \quad (8)$$

The CH_3N may form an addition product with the HCN as represented above; alternatively it may undergo a reorganisation, *e.g.*, into CH_2NH, the excitation energy sufficing to dissociate the methyl *iso*cyanate into hydrogen cyanide and formaldehyde. Reaction (8) may well be favoured by higher temperatures, and in addition the relative production of CH_3N in the primary act also increases. Polymerisation of CH_2NH can account for the heavy oil produced on photolysis at high temperatures. At lower temperatures the CH_3N mainly polymerises, or adds on to methyl *iso*cyanate, thus forming the cloud. Further, since no hydrogen is formed on irradiation with nitric oxide, even at high temperatures, it is reasonable to suppose that no formaldehyde is produced in these circumstances. (The argument that formaldehyde is formed, but escapes notice on account of reactions with nitric oxide, either before or after photolysis, is unsatisfactory. In the first place the volumes of nitric oxide used, given in Table II, do not permit of such reactions, and secondly, hydrogen is formed in the molecular condition by photolysis of formaldehyde, and hence is unlikely to react with nitric oxide.) These facts are explained if the aldehyde is formed by a reaction involving CH_3N, as in (8), for when nitric oxide is present, (5) occurs to the exclusion of (8). It does not therefore appear that dissociation into formaldehyde and hydrogen cyanide occurs when methyl *iso*cyanate molecules collide with excited mercury atoms.

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CAMBRIDGE. [*Received, November 20th*, 1940.]

* Norrish's figure of 101 kg.-cals. becomes 69 kg.-cals. if recalculated on the basis of more recent energy values of the C–H and H–H links.

9. *Triterpene Resinols and Related Acids. Part XII. The Oxidation of β-Amyradienyl-I Acetate with Selenium Dioxide, a New Route to Jacobs' Keto-diol,* $C_{30}H_{44-46}O_3$.

By C. W. Picard and F. S. Spring.

The preparation of β-amyradienol-I (III, R = H) from β-amyrenonol (II) is accompanied by the formation of β-amyradienol-II (IV). Oxidation of β-amyradienyl-I acetate (III, R = COMe) with selenium dioxide gives the keto-acetate $C_{32}H_{48(46)}O_4$ previously described by Jacobs and Fleck and by Simpson. With a view to determining the structure of the last-mentioned compound, β-amyrenonyl esters have been oxidised by bromine to the corresponding esters of β-*amyradienonol*, to which is ascribed the provisional structure (V). Oxidation of β-*amyradienonyl acetate* with potassium permanganate yields an *acetate*, $C_{32}H_{48}O_4$, which differs from Jacobs' keto-acetate.

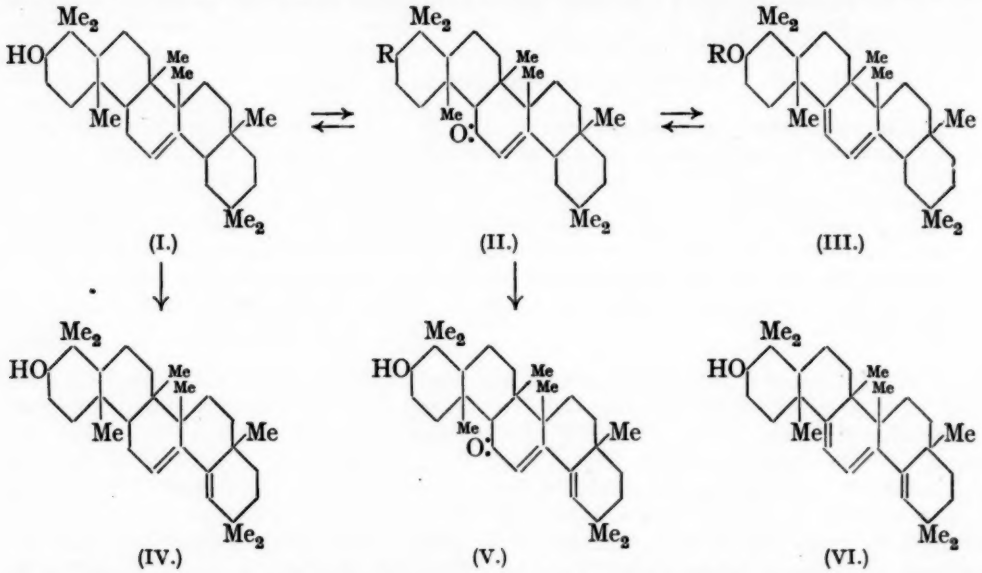
Reduction of β-amyrenonol with sodium and amyl or ethyl alcohol, followed by treatment of the intermediate addition-reduction compound with acetic anhydride, gives β-amyradienyl acetate, m. p. 216—217° (Picard and Spring, J., 1940, 1198). This compound and its derivatives are characterised by an absorption maximum at 2820 A., $\varepsilon_{max.} \simeq 10{,}000$, and by an extremely strong dextrorotation ($[\alpha]_D > 300°$). The parent alcohol we now designate β-amyradienol-I. From the mother-liquors of the product obtained by reduction of β-amyrenonol with sodium and amyl alcohol, we have now obtained an isomeric β-amyradienol, m. p. 227—228° (acetate, m. p. 226—227°), the absorption spectrum of which exhibits a major maximum at 2510 A. This compound is identical with the β-amyradienol obtained by oxidation of β-amyrenyl esters with selenium dioxide (Ruzicka, Müller, and Schellenberg, *Helv. Chim. Acta*, 1939, **22**, 767), which we now term β-amyradienol-II. β-Amyradienol-I contains its two ethylenic linkages as a conjugated system located in a single ring; the location of the absorption maximum of β-amyradienol-II indicates that the conjugated system is not contained in a single ring (cf. Ruzicka, Müller, and Schellenberg, *loc. cit.*).

An unsuccessful attempt was made to isomerise β-amyradienyl-I acetate to the isomeric dienyl-II acetate by treatment with mineral acids; the stability of the dienyl-I acetate was further demonstrated by its failure to react with bromine under a variety of experimental conditions. A satisfactory structural formulation of the two dienols is obtained in terms of the variant of the hydropicene triterpene formula suggested by Haworth (*Ann. Reports*, 1937, 338) [β-amyrenol = (I)] according to which β-amyrenonol will be (II, R = OH), the dienol-I (III, R = H), and the dienol-II (IV). Although these hypothetical formulæ represent the production of β-amyradienol-II (IV) from β-amyrenol (I) (by selenium dioxide oxidation) as the simple introduction of a conjugated ethylenic linkage, the formation of this dienol as a minor product of the reduction of β-amyrenonol (II, R = OH) requires a migration of ethylenic linkages.

In order to test these formulæ and at the same time accumulate further information about the immediate environment of the unsaturated centre in β-amyrenol, the oxidation of β-amyradienyl-I acetate (III, R = COMe) with selenium dioxide was examined; this reaction might be expected to yield a trienol (VI). The more soluble product of the oxidation is an acetate, $C_{32}H_{48}O_4$ (or $C_{32}H_{46}O_4$), m. p. 233—235°, hydrolysis of which gives the corresponding alcohol $C_{30}H_{46}O_3$ (or $C_{30}H_{44}O_3$), m. p. 286—287°. By direct comparison we find that this alcohol is identical with the keto-diol obtained by Jacobs and Fleck (*J. Biol. Chem.*, 1930, **88**, 137) by the oxidation of the thio-derivative of β-amyrenol, $C_{30}H_{44}OS$ (as benzoate) with potassium permanganate. The method of preparation of the keto-diol has been improved by Simpson (J., 1938, 1313; 1939, 755) and an examination of its reactions led this author to the view that it contains an isolated benzenoid ring; Ruzicka, Müller, and Schellenberg (*loc. cit.*) have shown this view to be untenable.

The less soluble product of the oxidation of the dienyl-I acetate is β-amyrenonyl acetate, m. p. 262—264° (II, R = O·COMe). We have previously shown that oxidation

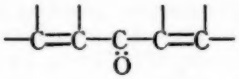
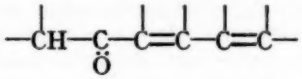
of β-amyradienol-I with chromic anhydride gives β-amyrenedione (Picard and Spring, *loc. cit.*), the conjugated system suffering 1 : 2-oxidation with formation of an αβ-un-

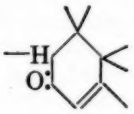
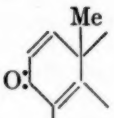
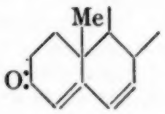


saturated ketonic system. This observation, together with the simultaneous formation of β-amyrenonyl acetate during the conversion of the dienyl-I acetate into Jacobs' ketodiol monoacetate, strongly suggested that the ketone group in the latter may originate in one of the ethylenic linkages of β-amyradienol-I. With this in mind, attempts have been made to introduce a second ethylenic linkage into β-amyrenonol and into *iso*-β-amyrenonol (Picard, Sharples, and Spring, J., 1939, 1045). In the first place it was observed that β-amyrenonyl and *iso*-β-amyrenonyl esters are not oxidised by selenium dioxide under conditions more drastic than those employed in the preparation of β-amyradienol-II. The desired oxidation, however, was readily effected when β-amyrenonyl benzoate was treated with bromine, reaction proceeding smoothly and giving *β-amyradienonyl benzoate*, m. p. 251—252°, in good yield. Hydrolysis of this ester gave *β-amyradienonol*, m. p. 239—240°, acetylation of which yielded *β-amyradienonyl acetate*, m. p. 255°. The latter ester is also obtained directly from β-amyrenonyl acetate by treatment with bromine.

The αβ-unsaturated ketone β-amyrenonyl acetate (II, R = O·COMe) exhibits an intense absorption maximum at 2450 A. β-Amyradienonyl acetate, on the other hand, exhibits an equally intense absorption maximum at 2815 A. The introduction of a second ethylenic linkage into β-amyrenonol by means of bromine could give rise to two different types of chromophoric group represented by (VII) and (VIII). The presence of the chromophore of type (VII) in a single six-membered ring produces an absorption maximum in the region 2300—2500 A.; thus 3-keto-$\Delta^{1:4}$-cholestadiene (Inhoffen and Huang-Minlon, *Ber.*, 1938, **71**, 1721) and santonin (Ruzicka, Cohen, Furter, and Sluys-Veer, *Helv. Chim. Acta*, 1938, **21**, 1735), each of which is represented by the partial structure (X), exhibit absorption maxima at approximately 2400 A. No data are available concerning the optical properties produced by this chromophoric type when it is distributed over two rings as in (XI). Turning now to the case of the chromophoric group (VIII), we have established that the saturated carbon atom adjacent to the carbonyl group in β-amyrenonol (II, R = OH) carries a hydrogen atom, since this αβ-unsaturated ketone can be converted into the conjugated β-amyradienol-I (III, R = H) and the latter is oxidised by chromic acid with re-formation of the αβ-unsaturated ketone group and simultaneous oxidation of the secondary alcohol group with the production of β-amyrenedione (II, R = O) (Picard and Spring, *loc. cit.*), thus proving that the formation of (III, R = H) from (II, R = OH) has been effected without the intervention of a retropinacolinic rearrangement.

Without making an assumption regarding the position of the extra-nuclear methyl group attachments in the β-amyrenol molecule, the unsaturated ring of β-amyrenonol is represented by (IX); the introduction of a second ethylenic linkage into (IX) to complete the chromophoric group (VIII) would produce a phenol. The presence in β-amyradienonol of the chromophoric group (VIII) located in a single ring system is excluded, since this dienonol does not exhibit phenolic properties either chemically or optically.

(VII.)   (VIII.)

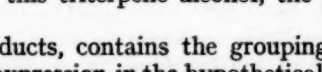
  

(IX.) (X.) (XI.) (XII.)

Polycyclic compounds containing the chromophoric group (VIII) distributed over two rings are well known; 3-keto-$\Delta^{4:6}$-cholestadiene (Dane, Wang, and Schulte, *Z. physiol. Chem.*, 1936, **245**, 80), 3 : 17-diketo-$\Delta^{4:6}$-androstadiene (Ruzicka and Bosshard, *Helv. Chim. Acta*, 1937, **20**, 328), 6-dehydrotestosterone, 6-dehydroprogesterone and 6-dehydrodeoxycorticosterone (Wettstein, *Helv. Chim. Acta*, 1940, **23**, 388), each of which contains the major chromophore (XII), all exhibit well-defined absorption maxima at approximately 2800 A. The influence of environment upon the chromophoric group (VIII) is emphasised in the case of the dienone prepared by pyrolysis of ketoacetyloleanolic acid (Ruzicka, Cohen, Furter, and Sluys-Veer, *loc. cit.*), which exhibits a maximum at 2975 A.

The absorption spectra of β-amyradienonyl esters strongly suggest that these contain the chromophoric group (VIII) but that this is not located in a single ring; the formula (I) for β-amyrenol being used, a satisfactory formulation (V) is obtained for β-amyradienonol.

Although the absorption spectrum of β-amyradienonyl acetate, $C_{32}H_{48}O_3$, is very similar to that of Jacobs' keto-diol monoacetate, $C_{32}H_{48(46)}O_4$, a very marked difference is to be observed in their reactions with tetranitromethane, the former giving a pronounced yellow coloration, whereas the latter (Simpson, *loc. cit.*), like β-amyrenonyl esters, fails to give a colour with this reagent. With a view to determining whether β-amyradienonol is related to Jacobs' keto-diol, the oxidation of the acetate of the former has been examined. β-Amyradienonyl acetate is resistant to oxidation by selenium dioxide, but is very readily oxidised by potassium permanganate to give an *acetate*, $C_{32}H_{48}O_4$, m. p. 233—235°. Although this acetate fails to give a coloration with tetranitromethane, it is different from Jacobs' keto-diol monoacetate, which has the same melting point.

A consideration of the series of step-wise oxidations of β-amyrenol represented at (I) ⟶ (V) shows that this triterpene alcohol, the parent of a considerable number of naturally occurring products, contains the grouping  , a fragment which finds expression in the hypothetical formula (I). The behaviour of *iso*-β-amyrenonyl acetate on treatment with bromine will be reported upon later.

Experimental.

β-*Amyradienol*-II.—The acetone mother-liquors obtained from the crystallisation of the addition-reduction compound $C_{35}H_{52}O_3$ (Picard and Spring, *loc. cit.*, p. 1201) (from 15 g. of β-amyrenonol) were combined, and the solvent removed; the solid (5·5 g.) in boiling alcohol (275 c.c.) was treated with sodium (15 g.), added during 30 minutes with vigorous stirring. The product was precipitated by the addition of water, collected, thoroughly washed with hot water, and dried. It was then heated with acetic anhydride (100 c.c.) and sodium acetate (1 g.) for 2 hours; the acetylated mixture was isolated by means of water and ether and fractionally crystallised from acetone. The top crop was repeatedly crystallised from the same solvent to yield β-amyradienyl-I acetate in needles, m. p. 213—214°; when mixed with an authentic specimen of the dienyl-I acetate, m. p. 216°, it melted at 214—216°. Hydrolysis

was effected by heating the acetate with 1% alcoholic potassium hydroxide solution for 5 hours. The product, isolated in the usual manner, after two crystallisations from methanol gave β-amyradienol-I in needles, m. p. 212—214°, undepressed by an authentic specimen. Concentration of the original acetone mother-liquor of the top crop gave a second crop of heavy plates, m. p. 218—220°; the remarkably sharp separation is to be ascribed to the fact that the minor component of the original mixture has a higher m. p. than the major component. After repeated crystallisation from acetone this crop gave β-amyradienyl-II acetate in plates, m. p. 226—227° (const.) either alone or when mixed with a specimen prepared by the selenium dioxide method (Ruzicka, Müller, and Schellenberg, *loc. cit.*). The dienyl-II acetate (0·1 g.) was heated under reflux with alcoholic potassium hydroxide (4%; 10 c.c.) for 2 hours. The mixture was diluted with water and extracted with ether, and the product crystallised from alcohol. Recrystallisation from the same solvent gave β-amyradienol-II in plates, m. p. 227—228°, undepressed by a specimen prepared by the method of Ruzicka, Müller, and Schellenberg (*loc. cit.*) but depressed to 200—210° by the parent acetate (Found: C, 84·7; H, 11·5. Calc. for $C_{30}H_{48}O$: C, 84·8; H, 11·4%). *Light absorption in alcohol:* Principal maximum, 2515 A., $\varepsilon_{max.}$ = 29,000; secondary maximum 2600 A., $\varepsilon_{max.}$ = 18,000. Both β-amyradienol-II and its acetate give a deep brown coloration with the tetranitromethane reagent.

Oxidation of β-Amyradienyl-I Acetate with Selenium Dioxide.—A boiling solution of the dienyl-I acetate (1·6 g.) in glacial acetic acid (50 c.c.) was treated during 1 hour with a solution of selenium dioxide (1·0 g.) in water (1 c.c.) and glacial acetic acid (50 c.c.). Sodium acetate (8 g.) was added, and the heating continued for 30 minutes. The selenium was removed, and the hot filtrate diluted with water and extracted with ether. The extract was washed with water and dried, removal of the solvent yielding a red resin. A solution of this in methanol deposited a top crop (A) (0·4 g.) of ill-defined crystals; concentration of the mother-liquor gave a second crop (B) (0·6 g.) of heavy plates. Each crop was contaminated with selenium and was difficult to crystallise.

β-Amyrenonyl Acetate.—The top crop (A) was refluxed with methyl-alcoholic potassium hydroxide solution (30 c.c.; 3%) for 2 hours; the solution was concentrated to 10 c.c., diluted with water, and extracted with ether. The ethereal solution was washed with water containing a trace of acetic acid, then with potassium carbonate solution, and dried. Removal of the solvent gave the hydrolysis product as a colourless solid, free from selenium. Crystallisation of the alcohol from the usual organic solvents was difficult because of its great solubility and the small amount of material available; it was therefore acetylated by heating on the steam-bath with pyridine (2 c.c.) and acetic anhydride (2 c.c.) for 1 hour. The acetylated product, isolated by means of ether, was thrice crystallised from acetone to give β-amyrenonyl acetate in prismatic needles, m. p. 262—264°, undepressed by the specimen described by Beynon, Sharples, and Spring (J., 1938, 1233); it did not give a coloration with tetranitromethane in chloroform and exhibited the typical light absorption properties of an αβ-unsaturated ketone (Found: C, 80·1; H, 10·8. Calc. for $C_{32}H_{50}O_3$: C, 79·6; H, 10·4%).

Jacobs' Keto-diol, $C_{30}H_{44(46)}O_3$.—Crop (B) was refluxed with methyl-alcoholic potassium hydroxide (40 c.c.; 3%) for 90 minutes. The solution was concentrated to approximately 10 c.c., diluted with water, and extracted with ether. On concentration of the dried extract the product separated in fine needles. Recrystallisation from light petroleum (b. p. 60—80°)–ether gave the keto-diol in needles, m. p. 286—287°, unchanged by subsequent recrystallisation from the same solvent. (From the first light petroleum mother-liquor, a second crop, m. p. 284—287°, was obtained.) A mixture of the keto-diol, m. p. 286—287°, with a specimen (m. p. 282—284°) prepared as described by Simpson (*loc. cit.*) had m. p. 285—286° (Found: C, 79·2; H, 10·1. Calc. for $C_{30}H_{46}O_3$: C, 79·25; H, 10·1. Calc. for $C_{30}H_{44}O_3$: C, 79·6; H, 9·8%). *Light absorption in alcohol:* Maximum at 2780 A., $\varepsilon_{max.}$ = 11,700. The keto-diol (0·1 g.), m. p. 286—287°, was heated on the water-bath for 2½ hours with pyridine (2 c.c.) and acetic anhydride (2 c.c.). The product, isolated in the usual manner, was crystallised twice from methanol, from which the keto-diol monoacetate separated in heavy plates, m. p. 233—235°, undepressed by a specimen prepared by Simpson's method (*loc. cit.*) (Found: C, 77·1; H, 9·8. Calc. for $C_{32}H_{48}O_4$: C, 77·4; H, 9·7. Calc. for $C_{32}H_{46}O_4$: C, 77·7; H, 9·4%). The keto-diol prepared by this method is more easily purified than that prepared from the thio-derivative of β-amyrenol.

β-Amyradienonyl Benzoate.—β-Amyrenonyl benzoate (Beynon, Sharples, and Spring, *loc. cit.*) (1 g.) in glacial acetic acid (30 c.c.) was treated with a solution of bromine in glacial acetic acid (3%; 11 c.c.) added dropwise at 85—95°. The bromine was rapidly absorbed and after the addition of approximately three-quarters of the bromine solution, crystals began to

separate from the hot solution. When the addition was complete, the solution was cooled, and the crystalline solid collected, washed with acetic acid, and thrice crystallised from the same solvent to give *β-amyradienonyl benzoate* in heavy lustrous plates, m. p. 251—252°. By combining and concentrating the acetic acid mother-liquors, a further quantity of the dienonyl benzoate was obtained (yield, 85%). It gave a yellow coloration with tetranitromethane in chloroform solution (Found: C, 81·6; H, 9·4. $C_{37}H_{50}O_2$ requires C, 81·9; H, 9·3%). *Light absorption in alcohol:* Maximum at 2835 A., $\varepsilon_{max.} = 12{,}000$. β-Amyradienonyl benzoate was recovered unchanged after heating with alcoholic hydroxylamine acetate for 5 hours.

β-Amyradienonol.—The benzoate (0·15 g.) was refluxed with alcoholic potassium hydroxide solution (7·5%; 15 c.c.) for 2 hours. After dilution with water, the solid was collected, washed with water, and thrice crystallised from methanol (in which it is moderately soluble), yielding *β-amyradienonol* in prismatic needles, m. p. 239—240° (Found: C, 81·6; H, 10·85. $C_{30}H_{46}O_2$ requires C, 82·1; H, 10·6%).

β-Amyradienonyl Acetate.—(a) β-Amyradienonol (0·25 g.) was heated on the steam-bath for 2 hours with pyridine (10 c.c.) and acetic anhydride (10 c.c.). After standing overnight, the solution was diluted with water, and the product collected and washed with water. After four crystallisations from methyl alcohol, *β-amyradienonyl acetate* separated in felted needles, m. p. 255° (Found: C, 79·7; H, 10·0. $C_{32}H_{48}O_3$ requires C, 80·0; H, 10·1%). *Light absorption in alcohol:* Maximum at 2815 A., $\varepsilon_{max.} = 14{,}000$.

(b) A solution of β-amyrenonyl acetate (Beynon, Sharples, and Spring, *loc. cit.*) (3 g.) in glacial acetic acid (120 c.c.) was treated at 70—75° with a solution of bromine in acetic acid (3%; 38·5 c.c.) added dropwise during 10 minutes. The bromine was rapidly absorbed with evolution of hydrogen bromide. After heating for a further 10 minutes, the solution was diluted with water, and the solid collected and washed with water. After four crystallisations from methyl alcohol containing a small amount of acetone, this gave β-amyradienonyl acetate in needles, m. p. 254—255°, unchanged by the specimen prepared by method (a).

Oxidation of β-Amyradienonyl Acetate.—A solution of potassium permanganate (1·1 g.) in water (22 c.c.) was added dropwise during 90 minutes to a solution of β-amyradienonyl acetate (1 g.) in stabilised glacial acetic acid (90 c.c.), the mixture being stirred throughout and the temperature maintained at 20°. After standing for 1 hour at the same temperature, the mixture was acidified with dilute sulphuric acid and clarified with sulphur dioxide. The precipitated solid was collected, washed with water, and crystallised from methanol and then from aqueous acetone, from which the *acetate* separated in plates, m. p. 234—235° (slight decomp.). When it was mixed with Jacobs' keto-diol monoacetate, m. p. 234—235°, the m. p. was depressed to 195—205°. The new acetate does not give a coloration with tetranitromethane in chloroform (Found: C, 76·8; H, 9·9. $C_{32}H_{48}O_4$ requires C, 77·4; H, 9·8%). *Light absorption in alcohol:* Maximum at 2470 A., $\varepsilon_{max.} = 10{,}000$.

Grateful acknowledgment is made to Dr. A. E. Gillam for many absorption spectrum determinations and to Mr. R. Sagar for making several of the experiments described.

THE UNIVERSITY, MANCHESTER. [*Received, November 25th*, 1940.]

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10. *The Cyclic Methyleneimines. Part III. Hydrolysis of Quaternary Compounds. Preparation of Secondary Amines.*

By JOHN GRAYMORE.

Hydrolysis of the products formed by the action of benzyl chloride on certain cyclic methyleneimines yielded a mixture of a secondary and a tertiary amine. With trimethyltrimethylenetriamine the quaternary compound *dibenzyldimethylammonium chloride* was obtained in addition. Ethyl bromide combines slowly with triethyltrimethylenetriamine. Allyl iodide reacts readily; acid hydrolysis of its addition product gave ethylallylamine and ethylamine.

IN previous work (Blundell and Graymore, J., 1939, 1787) it was shown that certain cyclic methyleneimines formed quaternary derivatives with alkyl iodides, but no reaction could be observed with alkyl chlorides.

The present communication deals with the action of benzyl chloride, ethyl bromide, and

allyl iodide on the bases. Addition of benzyl chloride took place readily, but the subsequent hydrolysis was attended by unexpected results in that with both the bases used it produced a tertiary amine in addition to the expected secondary amine. Further, trimethyltrimethylenetriamine also gave a good yield of *dibenzyldimethylammonium chloride*. The latter was isolated in the form of its *mercuric chloride* addition compound.

The addition product obtained from the methyl base with benzyl chloride separated in crystalline form. Analytical results on the product (washed free from the excess of benzyl chloride) indicated that it was a mixture. Hydrolysed by acid, it gave a mixture of the hydrochlorides of methylamine, benzylmethylamine, and benzyldimethylamine with dibenzyldimethylamine chloride. The formation of the amines could readily be accounted for by hydrolysis of the normal quaternary derivatives of the cyclic methyleneimine, but the appearance of a quaternary ammonium chloride amongst the products of hydrolysis suggested an addition of a further molecule of benzyl chloride, preceded by opening of the ring.

Attempts to separate the constituents of the addition products have failed, so the course of the reaction is still obscure.

Addition of allyl iodide to triethyltrimethylenetriamine took place rapidly. Acid hydrolysis of the product yielded ethylamine, ethylallylamine, and formaldehyde.

Combination of ethyl bromide with triethyltrimethylenetriamine and hydrolysis of the product follow the normal course; the yield is very small.

Experimental.

The analyses, due in the main to Drs. Weiler and Strauss, are micro-analyses.

Action of Benzyl Chloride on NN′N″-*Trimethyltrimethylenetriamine.*—To the base (30 g.), dried, redistilled, and cooled in ice–salt, benzyl chloride (29 g.) was gradually added. After 1 day a portion of the white crystalline product was washed with dry ether, and the ether removed in a vacuum, giving a mixture, m. p. 115—117° (Found: N, 15·7; Cl, 17·4. Calc. for $C_6H_{15}N_3,C_7H_7Cl$: N, 16·4; Cl, 13·9%. Calc. for $C_6H_{15}N_3,2C_7H_7Cl$: N, 11·0; Cl, 18·6%).

Hydrolysis of the addition product. A solution of the remainder of the product in hydrochloric acid was separated from unchanged chloride, steam-distilled to remove formaldehyde, and evaporated on the water-bath to incipient crystallisation. After rapid cooling, the crystals were removed and washed with warm chloroform, and the undissolved methylamine hydrochloride filtered off. The original mother-liquor, evaporated further, was thus gradually separated into a chloroform solution and a residue of methylamine hydrochloride (30 g.), m. p. and mixed m. p. 226°. The final residues did not crystallise but dissolved wholly in warm chloroform. The combined chloroform extracts on evaporation gave a thick syrup which did not crystallise. A solution of this in water was boiled to remove traces of chloroform and rendered alkaline with caustic soda. Ether then extracted a base (9 c.c.), b. p. 194—200°, which was shown to contain benzylmethylamine by formation of 2 : 4-dinitrobenzylmethylaniline, m. p. and mixed m. p. 141—142°. The remainder of the base was shaken with *p*-toluenesulphonyl chloride in alkali to remove the benzylmethylamine. The residual base was distilled into hydrochloric acid; the solution was evaporated to small bulk, and caustic soda added. The oil separating was isolated by means of ether and converted into benzyldimethylamine picrate, m. p. 94—95° (Found: N, 15·4. Calc. for $C_9H_{13}N,C_6H_3O_7N_3$: N, 15·4%).

Dibenzyldimethylammonium chloride. The liquor remaining after the ethereal extraction was made acid, and an excess of mercuric chloride solution added, giving a copious white precipitate, which crystallised from hot water in long needles, m. p. 167—168° (Found: C, 36·3; H, 3·6; Cl, 20·4; N, 2·7; Hg, 37·95. $C_{16}H_{20}NCl,HgCl_2$ requires C, 36·0; H, 3·6; Cl, 20·0; N, 2·6; Hg, 37·6%).

A solution of the product in hot water was freed from mercury by means of hydrogen sulphide, evaporated to small bulk, and then allowed to evaporate spontaneously. After some days large crystals were obtained. These were dissolved in acetone and shaken with anhydrous sodium carbonate (to remove the acid which persisted on recrystallisation from water); on evaporation of the acetone a liquid was obtained which crystallised in white plates, m. p. 85—90° (indistinct) (Found: Cl, 13·6. $C_{16}H_{20}NCl$ requires Cl, 13·6%).

Action of Benzyl Chloride on NN′N″-*Triethyltrimethylenetriamine.*—To the base (1 mol.), freshly distilled from barium oxide, benzyl chloride (1 mol.) was added slowly. Crystals separated at first, but gave place to a toffee-like mass. A solution of this in hydrochloric acid was

filtered from the unchanged chloride, steam-distilled to remove formaldehyde, evaporated to small bulk on the water-bath, and repeatedly extracted with ether after addition of caustic soda in excess. The ethereal layer, dried over barium oxide and distilled from a water-bath into hydrochloric acid, gave a residual oil and ethylamine hydrochloride (in the distillate). The residual oil had b. p. 194—200° (mainly 199—200°); dissolved in dry benzene, it was converted into a mixture of picrates (m. p. 80—110°). The picrates were separated by fractional crystallisation from hot alcohol, giving benzylmethylethylamine picrate, m. p. 113—114° (Found: N, 14·8. Calc. for $C_{10}H_{15}N,C_6H_3O_7N_3$: N, 14·8%), and *benzylethylamine picrate*, m. p. 122—123° (Found: C, 49·6; H, 4·6; N, 15·2. $C_9H_{13}N,C_6H_3O_7N_3$ requires C, 49·45; H, 4·4; N, 15·4%).

NN′N″-*Trimethyltrimethylenetriamine dichloride* was obtained by passing dry chlorine into the base in chloroform until a yellow colour began to develop. The dichloride was slowly deposited in short white needles after addition of ethyl acetate; m. p. 128—130° (decomp.) (Found: N, 20·7. $C_6H_{15}N_3Cl_2$ requires N, 21·0%). It decomposed in moist air, giving off formaldehyde.

Action of Allyl Iodide on Triethyltrimethylenetriamine.—To the base (9 g.), dissolved in dry ether (20 c.c.), allyl iodide (10 g.) was added. Separation of the addition product in white needles commenced at once. After 24 hours the mixture was treated with excess of hydrochloric acid, ether and unchanged allyl iodide separated, and the acid layer steam-distilled to remove formaldehyde. Evaporation to dryness was followed by extraction of the bases with ether after their liberation by concentrated sodium hydroxide solution. The ethereal solution was dried over barium oxide and distilled from a water-bath, the ethylamine being finally recovered as the hydrochloride (8 g.). Ethylallylamine (3 c.c.), b. p. 78—80°, was distilled after removal of the ether (Found: N, 16·5. Calc. for $C_5H_{11}N$: N, 16·5%).

Ethylallylamine picrate separated from a benzene solution of picric acid on addition of the base. Recrystallised from hot alcohol, it formed pale yellow rhomboids, m. p. 102° (Found: C, 42·5; H, 4·5; N, 17·7. $C_{11}H_{14}O_7N_4$ requires C, 42·4; H, 4·5; N, 17·8%).

Action of Ethyl Bromide on Triethyltrimethylenetriamine.—Ethyl bromide (10 c.c.) was added to the base (15 c.c.) in dry ether; the product, which separated slowly in white needles, was washed with dry ether and dried in a vacuum, giving a quaternary *compound*, m. p. 112—114° (decomp.), in 10% yield (Found: Br, 28·8. $C_{11}H_{26}N_3Br$ requires Br, 28·5%). On hydrolysis with hydrochloric acid and steam-distillation this gave ethylamine and diethylamine, identified by the derivatives formed with *p*-toluenesulphonyl chloride.

Thanks are expressed to the Chemical Society for a grant in aid of this research.

STOCKPORT COLLEGE. [*Received, July 27th,* 1940.]

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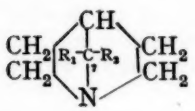
11. *Attempts to prepare 7-Substituted* bicyclo[1 : 2 : 2]-1-*Azaheptanes.*

By G. R. CLEMO and E. HOGGARTH.

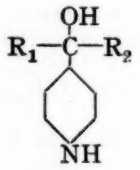
In order to prepare 7-methyl- and 7 : 7-dimethyl-*bicyclo*[1 : 2 : 2]-1-azaheptane the syntheses of methyl- and dimethyl-4-piperidylcarbinols have been investigated, but only the latter compound has been obtained. It was converted into 4-α-bromo*iso*propylpiperidine, which, however, could not be induced to lose hydrogen bromide in a manner which would form the desired bicyclic base.

BECAUSE of their relation to the camphane system, *bicyclo*[1 : 2 : 2]-1-azaheptanes with alkyl groups attached to the 7-carbon atom have considerable interest. Prelog and his co-workers have reported (*Chem. Centr.*, 1939, I, 2603) the failure of their method for the formation of this group of bicyclic bases in the case of (I; $R_1 = R_2 = Me$), although with some difficulty they prepared the monomethyl compound (I; $R_1 = Me$, $R_2 = H$). It was therefore considered desirable to apply the method used for the parent compound (Clemo and Metcalfe, J., 1937, 1523) to this problem. The preparation of the necessary piperidine alcohols (II; $R_1 = R_2 = Me$) and (II; $R_1 = Me$, $R_2 = H$) was attempted by way of the corresponding pyridyl alcohols. *Methyl-4-pyridylcarbinol* was prepared by the reduction of 4-acetylpyridine with aluminium *iso*propoxide or catalytically, and

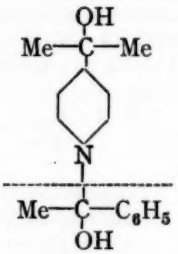
dimethyl-4-pyridylcarbinol by the action of methylmagnesium iodide on ethyl pyridine-4-carboxylate (Sobecki, *Ber.*, 1908, **41**, 4103; Emmert and Asendorf, *ibid.*, 1939, **72**, 1188).



(I.)



(II.)



(III.)

Both compounds were obtained in good yields, but they have resisted all attempts at hydrogenation either catalytically or by the Ladenburg method. The former, when platinum oxide or palladised charcoal in acetic acid, dilute hydrochloric acid, or acetic acid saturated with hydrogen chloride was used, always gave unchanged material, and 4-acetylpyridine yielded only methyl-4-pyridylcarbinol (compare Strong and McElvain, *J. Amer. Chem. Soc.*, 1933, **55**, 816). Dimethyl-4-pyridylcarbinol was recovered to the extent of 80% from sodium and alcohol reductions, together with a very small amount of a base, isolated only as its picrate. It seemed by analogy with the results of Sobecki (*loc. cit.*) that the latter would be 4-*iso*propylpyridine, and this was confirmed by its preparation from dimethyl-4-pyridylcarbinol by reduction with hydriodic acid and red phosphorus. The properties of this compound agreed with those given by Ladenburg (*Annalen*, 1888, **247**, 1), and the *picrate* was identical with that of the base obtained from the sodium and alcohol reduction. In order to eliminate the possibility of confusion with 4-α-*methylvinylpyridine*, which could be formed by dehydration, this compound was prepared by dehydration of dimethyl-4-pyridylcarbinol with phosphoric oxide, and its *picrate* shown to be quite distinct from the above. Methyl-4-pyridylcarbinol could not be reduced by the Ladenburg method and 4-ethylpyridine was not detected in the gummy product obtained.

Attention was next directed to the preparation of the piperidine alcohols from ethyl piperidine-4-carboxylate by means of the Grignard reaction, but in all cases bases as yet unidentified were isolated (Clemo and Metcalf, *loc. cit.*). Thus *ethyl* 1-*acetylpiperidine*-4-*carboxylate* gave, with methylmagnesium iodide, *dimethyl*-1-*acetyl*-4-*piperidylcarbinol*, which could not be deacetylated satisfactorily. The reaction of methylmagnesium iodide with ethyl 1-benzoylpiperidine-4-carboxylate was very complex, but gave the required compound in 6—7% yield. The gelatinous Grignard addition compound was decomposed in the usual way and small, roughly equivalent amounts of acetophenone and free *dimethyl*-4-*piperidylcarbinol* were at once liberated. These two compounds are probably formed by the decomposition of (III), produced by attack at both the ester and the benzoyl group of the starting material, and this view was strengthened by the isolation of appreciable amounts of piperidine and acetophenone when 1-benzoylpiperidine was subjected to the action of an excess of methylmagnesium iodide under similar conditions. Hydrolysis of the main fraction yielded approximately equivalent amounts of dimethyl-4-piperidylcarbinol and benzoic acid, but a considerable amount of material was left which was unchanged by prolonged boiling with acids or alkalis and its formation accounts for the low yield of the desired product. Varying the amount of the Grignard reagent and the temperature conditions were without significant effect on the proportions of the several substances formed.

By the action of hydrobromic acid on dimethyl-4-piperidylcarbinol, 4-α-*bromoisopropylpiperidine hydrobromide* was readily prepared, but when this compound was treated with alkali under conditions which converted 4-bromomethylpiperidine into the bicyclic base, the only product which could be isolated was dimethyl-4-piperidylcarbinol. Under anhydrous conditions with dry silver oxide or potassium carbonate there was obtained, in addition to small amounts of the same alcohol, an unsaturated secondary *amine*, $C_8H_{15}N$. This was

either an *iso*propyltetrahydropyridine or 4-*iso*propylidenepiperidine, since it was reduced catalytically to 4-*iso*propylpiperidine.

By the action of methylmagnesium iodide on ethyl piperidine-4-carboxylate a *base*, $C_7H_{13}ON$, was obtained in good yield. From the method of preparation this might be expected to be 4-acetylpiperidine. Prelog claims to have prepared this base (*Chem. Centr.*, 1939, I, 116) by the Claisen condensation of the benzoyl derivative of ethyl piperidine-4-carboxylate, but in only 5—10% yield; he does not describe it, and the properties of the derivatives he records do not agree with those found for our compounds. It is true it has not been possible to demonstrate the presence of a carbonyl group in our base, but the nitrogen atom has been methylated to give what appears to be 4-acetyl-1-methylpiperidine.

Experimental.

iso*Nicotinic Acid*.—This compound was prepared by the following modification of the method of Weidel and Herzig (*Monatsh.*, 1880, 1, 2). 2 : 4-Lutidine (30 g.) in water (3 l.) was stirred at 90° under a condenser, potassium permanganate (20 g.) added, a slow stream of carbon dioxide passed, and stirring continued until the colour was discharged. Fresh permanganate (20 g.) was added, and the process repeated until 250 g. in all had been introduced. The manganese dioxide was filtered off and washed with water, and the combined filtrates evaporated. The residue was made acid to Congo-red (50% hydrochloric acid) and evaporated nearly to dryness, and the paste dried in an open dish, coarsely powdered, and sublimed in superheated steam from a metal-bath at 300°/20—30 cm. The sublimate and yellowish distillate were united, a little concentrated hydrochloric acid added, and the whole evaporated under reduced pressure. The residue was basified (sodium hydroxide solution), and γ-picoline, formed presumably by decarboxylation of 4-methylpyridine-2-carboxylic acid, steam-distilled. The distillate was acidified (hydrochloric acid) and evaporated, the residue basified (sodium hydroxide), and the base taken up in chloroform, dried, and distilled. The fraction, b. p. 141—143°, was dissolved in hot alcohol (20—30 c.c.) and treated with a slight excess of picric acid. The picrate was washed with alcohol and by decomposition gave the base (2·2 g.), b. p. 142°, as a colourless oil. The picrate formed bright yellow clusters of needles, m. p. 166° (Found : C, 44·8; H, 3·5. Calc. for $C_6H_7N,C_6H_3O_7N_3$: C, 44·7; H, 3·2%), and the methiodide separated from dry acetone in colourless plates, m. p. 149° (Found : C, 35·4; H, 4·7. Calc. for $C_7H_{10}NI$: C, 35·7; H, 4·3%).

The alkaline residue from the steam-distillation was acidified (concentrated hydrochloric acid), reduced to 100 c.c., and cooled, and the sodium chloride filtered off and washed with a little 50% hydrochloric acid. The combined filtrates were evaporated and completely dried by the addition and removal in a vacuum of several small amounts of absolute alcohol. Thionyl chloride (80 c.c.) was added and when the reaction subsided the mixture was refluxed (8 hours), and the excess removed. The residue was treated with absolute alcohol (50 c.c.), refluxed for 2—3 hours, and the excess evaporated. Benzene (100 c.c.) was added, followed by sodium carbonate solution until the aqueous layer was alkaline; the benzene layer was removed, dried, and fractionated through a short column in a vacuum. The main fraction, b. p. 110—115°/15 mm., was a bright yellow oil, consisting almost entirely of ethyl pyridine-4-carboxylate. It was dissolved in methyl alcohol (20 c.c.), 50% aqueous potassium hydroxide (1 equiv.) added, and the mixture refluxed for 5 hours, neutralised with the calculated amount of hydrochloric acid, and evaporated to a paste in a vacuum. A little acetone was added, the solid collected and dried, and the *iso*nicotinic acid sublimed under reduced pressure from an oil-bath at 250°. The sublimate, crystallised once from water, gave white needles (9·3 g.), m. p. 311°. For the purposes described below, the uncrystallised sublimate, m. p. 302—303°, was sufficiently pure.

It was found possible to exercise some control over the relative amounts of *iso*nicotinic acid and γ-picoline obtained, by varying the amount of permanganate. Smaller amounts gave more γ-picoline, the highest yield (3·8 g.) being obtained when 130 g. were used. The amount of *iso*nicotinic acid was then much lower (3·2 g.) and appreciable amounts of lutidine escaped oxidation.

Ethyl Pyridine-4-carboxylate.—*iso*Nicotinic acid (12 g.) was refluxed with freshly purified thionyl chloride (50 c.c.) for 4—5 hours, the excess removed by distillation, and absolute alcohol (50 c.c.) cautiously added. After standing for a few minutes and refluxing for 2—3 hours, the mixture was worked up as described for the crude ester above. Ethyl pyridine-4-carboxylate was obtained as a clear liquid of characteristic unpleasant odour (11·5 g.), b. p. 113°/30 mm. The hydrochloride formed white deliquescent needles, m. p. 154° (Pinner, *Ber.*, 1901, 34, 4234,

gives 167°), which easily sublimed in a vacuum (Found: C, 50·3; H, 5·5. Calc. for $C_8H_9O_2N$,HCl: C, 50·1; H, 5·3%). The *picrate* formed yellow needles, m. p. 142° (Found: C, 44·5; H, 3·1. $C_8H_9O_2N,C_6H_3O_7N_3$ requires C, 44·2; H, 3·2%).

Dimethyl-4-pyridylcarbinol.—A Grignard solution prepared from magnesium (10 g.) and methyl iodide (20 c.c.) in ether (200 c.c.) was evaporated to remove the excess of methyl iodide, the residue taken up in ether (200 c.c.), and the filtered solution cooled to −10°, stirred, and treated with a solution of ethyl pyridine-4-carboxylate (12 g.) in ether (100 c.c.) during 1 hour. After 2 hours' stirring at −10°, the solution was refluxed for 5 hours and cooled, and the addition compound decomposed with ice and acetic acid. The ether was distilled off, the residue basified (sodium carbonate solution), and the oil extracted with chloroform, dried, and fractionated in a vacuum. Dimethyl-4-pyridylcarbinol was obtained as a colourless oil, b. p. 136°/25 mm., solidifying to a colourless crystalline solid (7·5 g.), which gave colourless needles, m. p. 132°, from benzene, freely soluble in alcohol or chloroform but sparingly in water or ether (Found: C, 70·1; H, 8·2. Calc. for $C_8H_{11}ON$: C, 70·0; H, 8·1%). No derivatives of this compound have been described previously. Emmert and Asendorf (*loc. cit.*) give only the m. p. of the compound (135°). The *picrate* separated from benzene as a yellow oil which slowly solidified and crystallised from benzene in slender, light yellow needles, m. p. 95° (Found: C, 46·3; H, 3·9. $C_8H_{11}ON,C_6H_3O_7N_3$ requires C, 45·9; H, 3·9%). The *picrolonate* formed slender yellow needles, decomp. 236°, which contained a molecule of alcohol of crystallisation (Found: C, 53·7; H, 5·5. $C_8H_{11}ON,C_{10}H_8O_5N_4,C_2H_6O$ requires C, 53·7; H, 5·6%). The *platinichloride* separated from dilute hydrochloric acid, on addition of alcohol, in golden-yellow plates, m. p. 194°, very soluble in water or alcohol (Found: C, 28·3; H, 3·4; Pt, 28·6. $2C_8H_{11}ON,H_2PtCl_6$ requires C, 28·1; H, 3·5; Pt, 28·5%).

Attempted Reduction of Dimethyl-4-pyridylcarbinol by Sodium and Alcohol.—A solution of the above compound (5 g.) in dry amyl alcohol or absolute alcohol (500 c.c.) was refluxed whilst sodium (50 g.) was cautiously added during 3 hours. When all the sodium had dissolved, the liquid was diluted with an equal volume of water, acidified (concentrated hydrochloric acid), and evaporated to 100 c.c. The sodium chloride was filtered off and washed with a little 50% hydrochloric acid and the combined filtrates were evaporated, basified with sodium hydroxide solution, and extracted with chloroform. Distillation in a vacuum yielded an oil (0·2 g.), b. p. 65—75°/15 mm., and dimethyl-4-pyridylcarbinol (3·8 g.). The oil had a powerful and distinctive odour and gave a light yellow picrate, m. p. 134°, identical with that of 4-*iso*propylpyridine (*v. infra*) (Found: C, 47·8; H, 4·1%).

4-iso*Propylpyridine.*—Dimethyl-4-pyridylcarbinol (0·7 g.), red phosphorus (1·4 g.), and hydriodic acid (6 c.c., *d* 1·7) were heated in a sealed tube at 140° for 60 hours. The resulting clear liquid was evaporated, the residue basified (sodium carbonate solution), and the liberated oil taken up in ether and distilled. The main fraction (b. p. 70—72°/21 mm.) was converted into the picrolonate and recovered, giving a colourless oil of pleasant odour (0·4 g.), b. p. 173°/760 mm., which was stable to alkaline permanganate (Found: C, 79·0; H, 9·4. Calc. for $C_8H_{11}N$: C, 79·3; H, 9·2%). The *picrate* separated from alcohol in small, light yellow needles, m. p. 135° (Found: C, 48·1; H, 4·3. $C_8H_{11}N,C_6H_3O_7N_3$ requires C, 48·0; H, 4·0%), and the platinichloride from dilute hydrochloric acid in golden-yellow plates, m. p. 202° (Found: C, 29·6; H, 4·1; Pt, 29·9. Calc. for $2C_8H_{11}N,H_2PtCl_6$: C, 29·4; H, 3·7; Pt, 30·0%). The *picrolonate* formed long, deep yellow needles, m. p. 208° (Found: C, 56·2; H, 5·2. $C_8H_{11}N,C_{10}H_8O_5N_4$ requires C, 56·1; H, 5·0%).

α-Methylvinylpyridine.—Dimethyl-4-pyridylcarbinol (1·0 g.) and phosphoric oxide (3 g.) were gradually heated to 80—85° in a sealed tube and held at this temperature for ½ hour. A little ice was added, followed by sodium hydroxide solution, and the base was distilled in steam. The distillate (75—100 c.c.) was acidified (concentrated hydrochloric acid) and evaporated to dryness, and the base liberated (sodium hydroxide solution) and extracted with ether. The dried filtered solution was added to a warm solution of picric acid (1·0 g.) in alcohol. The picrate was collected and decomposed (50% hydrochloric acid), giving 4-*α-methylvinylpyridine* as a colourless oil of strong pleasant odour, b. p. 82°/15 mm. (Found: C, 80·3; H, 7·4. C_8H_9N requires C, 80·6; H, 7·6%). It rapidly decolourised bromine water and neutral permanganate, was strongly alkaline to litmus, and was miscible with most organic solvents. The *picrate* separated from alcohol in felted needles containing a molecule of alcohol of crystallisation (Found: C, 49·2; H, 4·9. $C_8H_9N,C_6H_3O_7N_3,C_2H_6O$ requires C, 48·8; H, 4·6%). The *picrolonate* crystallised from alcohol in slender yellow needles, m. p. 231° (discoloured at 225°) (Found: C, 56·3; H, 4·7. $C_8H_9N,C_{10}H_8O_5N_4$ requires C, 56·4; H, 4·5%).

4-*Acetylpyridine.*—The method used was a modification of that given by Pinner (*Ber.*, 1901,

34, 4234). The 4-acetylpyridine was obtained as a colourless oil (2·5 g.) of pleasant odour, b. p. 106°/25 mm. (Found : C, 69·1; H, 6·0. Calc. for C_7H_7ON : C, 69·4; H, 5·9%). The picrate separated from alcohol in bright yellow needles, m. p. 128° (Found : C, 44·6; H, 3·1. Calc. for $C_7H_7ON,C_6H_3O_7N_3$: C, 44·6; H, 2·9%).

Methyl-4-pyridylcarbinol.—(a) 4-Acetylpyridine (1·0 g.) and aluminium *iso*propoxide (4 g.) in dry *iso*propyl alcohol (20 c.c.) were boiled under a short fractionating column until the distillate was free from acetone as tested for with 2 : 4-dinitrophenylhydrazine (2½—3 hours). The excess of the reagent was decomposed (50% hydrochloric acid, 50 c.c.), the solution evaporated to a paste, and the base liberated (sodium carbonate solution), extracted with chloroform, and distilled, giving a colourless oil (0·75 g.), b. p. 138—140°/30 mm., which solidified slowly over phosphoric oxide in a desiccator. The colourless *solid* crystallised from light petroleum (b. p. 40—60°)–benzene in large deliquescent prisms, m. p. 54°, very easily soluble in most organic solvents (Found : C, 68·3; H, 7·1. C_7H_9ON requires C, 68·2; H, 7·4%).

(b) 4-Acetylpyridine (1·0 g.) gave 0·8 g. of the above base when reduced catalytically (Found : C, 68·4; H, 7·3%).

The *picrate* of methyl-4-pyridylcarbinol separated from dry benzene in slender, sulphur-yellow needles which darkened in the light; m. p. 125° (Found : C, 43·9; H, 3·4. $C_7H_9ON,C_6H_3O_7N_3$ requires C, 44·3; H, 3·4%). The *picrolonate* was obtained from alcohol in yellow leaflets, m. p. 232° (Found : C, 52·5; H, 4·1. $C_7H_9ON,C_{10}H_8O_5N_4$ requires C, 52·7; H, 4·4%). The *platinichloride* separated from dilute hydrochloric acid, on addition of a little alcohol, in deep golden-yellow prisms, m. p. 206° (Found for material dried in a vacuum at 120° : C, 25·3; H, 2·9; Pt, 29·8. $2C_7H_9ON,H_2PtCl_6$ requires C, 25·6; H, 3·1; Pt, 29·8%).

Ethyl 1-*Acetylpiperidine-4-carboxylate.*—Ethyl piperidine-4-carboxylate (5 g.) in dry chloroform (30 c.c.) was cooled in ice, and an ice-cold solution of acetyl chloride (5 c.c.)in chloroform (30 c.c.) cautiously added. The mixture was treated with anhydrous potassium carbonate (10 g.), the whole refluxed for 1 hour, and the liquid filtered and distilled. The main fraction (6 g., b. p. 135—136°/1 mm.) was a colourless oil which did not crystallise (Found : C, 60·0; H, 8·8; N, 7·4. $C_{10}H_{17}O_2N$ requires C, 60·3; H, 8·6; N, 7·0%).

Reaction of Methylmagnesium Iodide with Ethyl 1-*Acetylpiperidine-4-carboxylate.*—The above acetyl compound (5 g.) in absolute ether (30 c.c.) was cooled in ice and stirred while a Grignard solution, prepared from magnesium (10 g.) and methyl iodide (28 c.c.) in ether (60 c.c.) and purified as described previously, was slowly dropped in. The grey viscid mass, after standing in the ice overnight, was boiled for a few minutes and then decomposed with ice and acetic acid. The ether was removed, and the residue basified (sodium hydroxide solution) and extracted with chloroform. The oil remaining after removal of the solvent was treated with absolute alcohol (10 c.c.) and kept in a refrigerator for a few days. The colourless crystalline solid which separated was collected and recrystallised from alcohol. This compound (0·5 g.), m. p. 233°, has not been identified; it formed long silky needles which sublimed easily in a vacuum and readily dissolved in water, giving a neutral solution (Found : C, 68·0, 67·8; H, 9·8, 9·85%). The alcoholic mother-liquor from the initial crystallisation of this substance yielded *dimethyl*-1-*acetyl*-4-*piperidylcarbinol* as a colourless oil (2·5 g.), b. p. 162—165°/1 mm., which did not crystallise on standing (Found : C, 64·6; H, 10·7; N, 7·7. $C_{10}H_{19}O_2N$ requires C, 64·8; H, 10·4; N, 7·6%). The compound was not attacked by alcoholic potash or concentrated hydrochloric or hydrobromic acid during 2—3 hours' boiling. Further boiling resulted in the formation of a brown gum from which nothing definite could be isolated.

Ethyl 1-*Benzoylpiperidine-4-carboxylate.*—Ethyl piperidine-4-carboxylate (14 c.c.) in chloroform (40 c.c.) was treated with benzoyl chloride (12·8 c.c.) in chloroform (20 c.c.) with cooling. Anhydrous potassium carbonate (20 g.) was added, the mixture refluxed for 4 hours, and the liquid filtered and fractionated in a vacuum. The fraction, b. p. 190—195°/1 mm., slowly set to a white crystalline solid (18—20 g.), m. p. 60—65°, which was pure enough for subsequent experiments. Crystallisation from benzene–light petroleum gave stout pointed needles, m. p. 77°, very soluble in alcohol but sparingly soluble in ether (Found : C, 69·1; H, 7·4. Calc. for $C_{15}H_{19}O_3N$: C, 68·9; H, 7·3%).

Reaction of Methylmagnesium Iodide with Ethyl 1-*Benzoylpiperidine-4-carboxylate.*—The treatment of the above benzoyl compound (12 g.) in ether (200 c.c.) and chloroform (50 c.c.) with a purified Grignard solution prepared from magnesium (36 g.) and methyl iodide (80 c.c.) in dry ether (250 c.c.) and the subsequent procedure (3 hours' boiling instead of a few minutes) were the same as those described for the acetyl analogue. The oil finally obtained from the chloroform extract was fractionated in a vacuum. Two main fractions were taken : (A) 0·9—1·0 g., b. p. 80—120°/1 mm.; (B) 5·5—6·0 g., b. p. 175—195°/1 mm. The considerable residue

of organic material crystallised from ethyl acetate in faintly yellow plates, m. p. 205—206° (Found : C, 73·6, 74·1; H, 7·0, 7·5; N, 10·2%). Fraction (A) was dissolved in dilute hydrochloric acid (20 c.c.), the liquid evaporated, and the distillate extracted with ether; distillation of the dried extracts gave acetophenone (0·3 g., b. p. 92—93°/15 mm.), identified as the semicarbazone, m. p. 201°, and the oxime, m. p. 59°, not depressed by authentic specimens. The residue from the evaporation of the acid solution was basified (sodium hydroxide solution) and extracted with chloroform and the oil left after evaporation of the dried extracts was distilled in a vacuum. The product (0·2 g., b. p. 140—143°/25 mm.) solidified on cooling and crystallised in long needles, m. p. 136°, identical with the base prepared by hydrolysing the main fraction (below) (Found : C, 67·2; H, 11·5%). Fraction (B) was dissolved in alcohol (20 c.c.), treated with potassium hydroxide (3·0 g.) in 50% alcohol (20 c.c.), and the mixture refluxed for 6—8 hours. The *dimethyl-4-piperidylcarbinol* was removed in steam, the distillate (400—450 c.c.) acidified (concentrated hydrochloric acid) and evaporated, and the base recovered as a colourless oil, b. p. 140—142°/25 mm., rapidly setting to a crystalline solid (0·6 g.), m. p. 132°. Crystallisation from benzene–light petroleum (b. p. 60—80°) or sublimation from the water-bath gave colourless silky needles, m. p. 136° (Found : C, 67·1; H, 11·6; N, 10·2. $C_8H_{17}ON$ requires C, 67·1; H, 11·9; N, 9·8%). The *picrate* was obtained in dimorphic modifications, one of which, light yellow prisms, m. p. 156° (Found : C, 45·0; H, 5·5. $C_8H_{17}ON,C_6H_3O_7N_3$ requires C, 45·1; H, 5·4%), could be converted into the other, deep golden-yellow needles, m. p. 187° (Found : C, 45·2; H, 5·6%), by solution in alcohol and seeding. The *picrolonate* formed clusters of light yellow needles, m. p. 265° (decomp.), from alcohol (Found : C, 53·1; H, 6·0. $C_8H_{17}ON,C_{10}H_8O_5N_4$ requires C, 53·0; H, 6·2%). Fraction (B) contained, in addition to dimethyl-1-benzoyl-4-piperidylcarbinol, a considerable amount of organic material resistant to hydrolysis. The alkaline residue from the steam-distillation of dimethyl-4-piperidylcarbinol was extracted with chloroform and the oil remaining after removal of the solvent was fractionated through a short column in a vacuum. Two substances were isolated; the first, obtained by many distillations of a fraction, b. p. 175—180°/1 mm., was a colourless viscid oil, b. p. 176°/1 mm. (Found : C, 73·8; H, 8·1; N, 6·7%), and the second, obtained in a similar manner from the fraction, b. p. 195—198°/1 mm., was a faintly yellow liquid which slowly solidified to a colourless crystalline mass, m. p. 25—30° (Found : C, 71·3; H, 8·1; N, 6·3%). These compounds were obtained in approximately equal amounts (2·5 g.).

4-α-*Bromoisopropylpiperidine Hydrobromide*.—Dimethyl-4-piperidylcarbinol (1·0 g.) and hydrobromic acid (10 c.c., *d* 1·7) were refluxed for 15 minutes, and the excess of acid at once removed under reduced pressure. The solid residue crystallised from absolute alcohol in colourless plates (1·4 g.), m. p. 192° (Found : C, 33·5; H, 5·9; N, 4·9. $C_8H_{16}NBr,HBr$ requires C, 33·5; H, 6·0; N, 4·9%).

Reaction of 4-α-*Bromoisopropylpiperidine Hydrobromide with Silver Oxide*.—The above hydrobromide (1 g.) and dry, freshly prepared silver oxide (2·0 g.) were cautiously mixed in a mortar and sealed up in a number of small thick-walled tubes. Each was gently warmed in the water-bath until a vigorous reaction took place, then heated for ½ hour longer and allowed to cool, and the contents washed out with a little water. The united product was basified (concentrated sodium hydroxide solution) and distilled in steam. The distillate was acidified (concentrated hydrochloric acid) and evaporated to dryness, and the residue basified (sodium hydroxide solution) and extracted with ether. The solvent was removed, light petroleum (b. p. 40—60°, 2 c.c.) added, and the mixture kept at 0° for 12 hours. The small amount of dimethyl-4-piperidylcarbinol was filtered off, and the filtrate distilled, giving a colourless *oil* (0·1 g.), b. p. 58—62°/12 mm. (Found : C, 76·3; H, 11·9. $C_8H_{15}N$ requires C, 76·7; H, 12·1%). The *picrolonate* separated from alcohol in deep yellow prisms, m. p. 221° (Found : C, 55·6; H, 6·2. $C_8H_{15}N,C_{10}H_8O_5N_4$ requires C, 55·5; H, 6·0%).

4-iso*Propylpiperidine*.—The above base (0·1 g.) in glacial acetic acid (5 c.c.) was shaken for 12 hours with platinum oxide (0·01 g.) in hydrogen at 100 lb./sq. in. The liquid was filtered, acidified with a few drops of concentrated hydrochloric acid, and evaporated, and the base recovered as a colourless oil (0·08 g.) of strong unpleasant smell, b. p. 66—70°/15 mm., completely miscible with water, giving a strongly alkaline solution (Found : C, 75·5; H, 12·9. Calc. for $C_8H_{17}N$: C, 75·6; H, 13·4%). The platinichloride separated from dilute hydrochloric acid, on addition of a little alcohol, in orange leaflets, m. p. 182° (Found for material dried at 100°/15 mm. : C, 28·7; H, 5·2; Pt, 29·6. Calc. for $2C_8H_{17}N,H_2PtCl_6$: C, 28·9; H, 5·4; Pt, 29·4%).

Reaction of Ethyl Piperidine-4-carboxylate with Methylmagnesium Iodide.—To a Grignard reagent prepared from magnesium (8 g.) and methyl iodide (25 c.c.), purified in the usual way,

and dissolved in ether (150 c.c.), a solution of ethyl piperidine-4-carboxylate (6 c.c.) in ether (100 c.c.) was slowly added with stirring at − 15°. The mixture was kept at 0° for 12 hours, then cooled strongly and decomposed with ice and acetic acid. The ether was removed on the water-bath, and the residue basified (concentrated sodium hydroxide) and distilled in steam. The steam-distillate (300—350 c.c.) was acidified to Congo-red (concentrated hydrochloric acid) and evaporated under reduced pressure, and the *base* liberated by potassium carbonate solution, extracted with ether, and distilled, giving a colourless oil of pleasant odour (2·5 g.), b. p. 108—110°/25 mm. (Found: C, 66·1, 65·9; H, 11·1, 10·9; N, 11·1. $C_7H_{13}ON$ requires C, 66·1; H, 10·3; N, 11·0%). The *picrate* separated slowly from alcohol in stout yellow needles, m. p. 266° (decomp.) (Found: C, 43·9; H, 4·5. $C_7H_{13}ON,C_6H_3O_7N_3$ requires C, 43·8; H, 4·5%). The *picrolonate* formed small, deep yellow prisms, m. p. 206°, from alcohol (Found: C, 52·3; H, 5·3. $C_7H_{13}ON,C_{10}H_8O_5N_4$ requires C, 52·1; H, 5·4%). The *platinichloride* formed small, deep orange prisms, m. p. 206°, from dilute hydrochloric acid and alcohol (Found: C, 27·0; H, 4·1; Pt, 27·7. $2C_7H_{13}ON,H_2PtCl_6,C_2H_6O$ requires C, 27·0; H, 4·8; Pt, 27·5%). Nothing definite was isolated in attempts to prepare, by the usual methods, the oxime, hydrazone, semicarbazone or phenylhydrazone. The base was recovered unchanged and identified by its picrolonate after treatment with excess of methylmagnesium iodide and after boiling for as long as 84 hours with amalgamated zinc and concentrated hydrochloric acid. The compound also distilled unchanged from zinc dust, gave no acetone on boiling with aluminium *iso*propoxide, and no detectable absorption of hydrogen was noted on shaking with a platinum catalyst in acetic acid. On treatment with phosphorus pentachloride in chloroform a violent reaction took place and the mixture rapidly darkened; nothing definite could be obtained after basification with potassium carbonate and extraction with chloroform. By treating the reaction mixture with 50% hydrochloric acid and granulated tin a small amount of unchanged base was recovered, identified as picrolonate (0·01 g., m. p. 205°, from 0·2 g. of the base). On treatment with methyl iodide a vigorous reaction took place with formation of a gum which crystallised from acetone in colourless prisms, m. p. 170° (after sintering at 152°) (Found: C, 35·7; H, 5·4. $C_7H_{13}ON,CH_3I$ requires C, 35·7; H, 5·9%). This *compound* (0·25 g.) was dissolved in water and treated with freshly prepared silver oxide (2·5 g.); an oil, b. p. 108—109°/25 mm., was obtained by chloroform extraction (Found: C, 67·8; H, 11·1. $C_8H_{15}ON$ requires C, 68·1; H 10·6%). The *picrolonate* of this base formed light yellow leaflets. m. p. 215° (Found: C, 53·1; H, 5·8. $C_8H_{15}ON,C_{10}H_8O_5N_4$ requires C, 53·3; H, 5·7%).

One of us (E. H.) thanks Durham County Council for a Senior Exhibition.

UNIVERSITY OF DURHAM, KING'S COLLEGE,
NEWCASTLE-UPON-TYNE, 2.

[*Received, October 21st*, 1940.]

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12. *The Action of Periodic Acid on Glucosamine Derivatives.*

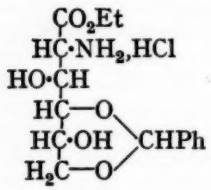
By ALBERT NEUBERGER.

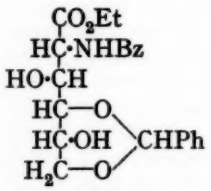
The action of periodic acid on derivatives of glucosamine and glucosamic acid has been investigated. In the latter case the oxygen uptake exceeds the theoretical value, unless the hydroxyl adjacent to the amino-group is blocked. For *N*-acylglucosaminides the oxygen uptake is normal, if metaperiodate is used. Free periodic acid, however, gives too high results and leads to secondary decomposition.

THE original purpose of investigating the action of periodic acid on derivatives of glucosamine was to convert this amino-sugar into an amino-acid occurring in proteins for which the *l*-configuration has been well established and thus to demonstrate the configurational relationship between amino-acids and amino-sugars. This aim has not been attained, but certain observations have been made which show that periodic acid may be a useful tool for structural studies involving these compounds.

Karrer and Mayer (*Helv. Chim. Acta*, 1937, **20**, 407), starting from a compound first prepared by Levene and La Forge (*J. Biol. Chem.*, 1915, **21**, 348) and considered by the latter authors to be ethyl 5 : 6-benzylidene glucosamate hydrochloride, attempted to oxidise its *N*-carbethoxy-derivative between carbon atoms 3 and 4, using lead tetra-acetate.

Fission, however, took place between carbon atoms 2 and 3, leading to a glyoxylic acid–ammonia derivative. The formula of a 4 : 6-benzylidene compound was therefore assigned to the substance of Levene and La Forge (I).


(I.)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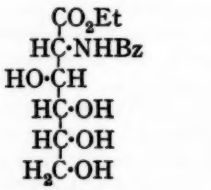
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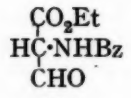
(IV.)

It was thought that the desired substituted amino-aldehyde might be obtained by removing the benzylidene residue and treating the resulting compound, which has four neighbouring hydroxyl groups, with either lead tetra-acetate or periodic acid. (I) was therefore benzoylated to give *ethyl* N-*benzoyl* 4 : 6-*benzylidene glucosamate* (II), from which on catalytic hydrogenation *ethyl* N-*benzoyl glucosamate* (III) was obtained. It was expected that on treatment with lead tetra-acetate (III) would use up three atoms of oxygen to produce (IV), two mols. of formic acid and one mol. of formaldehyde. It was found, however, that more than 4·5 mols. of oxygen were used up and that complete destruction of the molecule had taken place. Treatment of (III) with periodic acid or sodium metaperiodate also leads to an excessive uptake of oxygen and moreover to a liberation of iodine and ammonia. It is probable that the α-benzamido-aldehyde (IV) first formed is too unstable and/or is further oxidised and polymerised. Glucosamic acid itself behaves in a similar manner towards periodic acid.

If the hydroxyl group in position 3 is blocked as in 3-methylglucosamic acid (following paper), the oxygen uptake is normal: two equivalents of periodic acid are taken up and one mol. of formaldehyde and one mol. of a volatile reducing acid, presumably formic acid, are formed. An attempt to isolate the β-amino-aldehyde, the presumed reaction product, in the form of its hydrochloride was unsuccessful, nor was a catalytic reduction with platinum and ferric chloride (Carothers and Adams, *J. Amer. Chem. Soc.*, 1923, **45**, 1071) to the corresponding 2-amino-4-hydroxy-3-methoxybutyric acid possible.

The behaviour of *N*-acylglucosaminides towards metaperiodate is more normal. *N*-Acetyl-α-methylglucosaminide (Moggridge and Neuberger, J., 1938, 745), which has one pair of hydroxyl groups attached to adjacent carbon atoms, takes up one atom of oxygen with sodium metaperiodate; the reaction is slow, which is probably due to the fact that the two hydroxyl groups are in the *trans*-position to each other. If free periodic acid, however, is used, the oxygen uptake reaches two equivalents in 22 hours and iodine is liberated. Identical results were obtained with N-*benzoyl-α-methylglucosaminide* which was prepared from *N*-benzoyl tetra-acetyl glucosamine (Bergmann and Zervas, *Ber.*, 1931, **64**, 975) by treatment with 2·1% methyl-alcoholic hydrogen chloride. The dialdehyde presumably formed on treating the *N*-acylglucosaminides with sodium metaperiodate could not be isolated, nor could any dicarboxylic acids or their calcium and barium salts be obtained after oxidising the crude reaction products with bromine at p_H 5 or perbenzoic acid.

If, however, the hydroxyl group in position 3 is blocked as in 3-methyl *N*-acetyl α-methylglucosaminide (following paper), no oxygen uptake with either periodic acid or sodium metaperiodate occurs. It may be assumed that similarly no reaction will occur if position 4 is substituted, since it has been found that a hydroxyl group adjacent to a carbon atom to which an acylamido-group is attached reacts with periodic acid only very slowly, if at all (Nicolet and Shinn, *J. Amer. Chem. Soc.*, 1939, **61**, 1615).

The usefulness of sodium metaperiodate as a tool for elucidating the structure of a partially substituted glucosaminide is shown in the following paper; the results here reported may also help to explain the experiments on the oxidation of heparin by periodate (Charles and Todd, *Biochem. J.*, 1940, **34**, 112).

Experimental.

Ethyl N-*Benzoyl* 4 : 6-*Benzylidene Glucosamate.*—To ethyl 4 : 6-benzylidene glucosamate hydrochloride (3·6 g.), dissolved in water (40 ml.) containing sodium bicarbonate (1·95 g.), benzoyl chloride (1·35 ml.) was added in small portions during ½ hour; the mixture was shaken intermittently and kept at 5°. The crystalline precipitate which separated at once was filtered off and recrystallised first from chloroform and light petroleum (b. p. 60—80°) and then from alcohol; m. p. 173—174°, $[\alpha]_D$ −80° in chloroform (c = 1·1) (Found: C, 63·4; H, 5·9; N, 3·4. $C_{22}H_{25}O_7N$ requires C, 63·6; H, 6·0; N, 3·4%).

Ethyl N-*Benzoyl Glucosamate.*—Ethyl *N*-benzoyl 4 : 6-benzylidene glucosamate (2·7 g.), dissolved in alcohol (50 ml.), was treated with palladium (0·7 g.) and hydrogen for 6 hours; 4 atoms of hydrogen per mol. had then been taken up. The catalyst was filtered off, and the solution evaporated to low bulk. On addition of ether the *substance* crystallised in needles (yield, 70%), m. p. 144—145°, $[\alpha]_D$ + 11·8° in water (c = 0·8) (Found: C, 55·0; H, 6·3; N, 4·3. $C_{15}H_{21}O_7N$ requires C, 55·1; H, 6·4; N, 4·3%).

N-*Benzoyl* α-*Methylglucosaminide.*—*N*-Benzoyl tetra-acetyl glucosamine (23 g.) was refluxed with 2·1% methyl-alcoholic hydrogen chloride for 2 hours. The excess of acid was removed by lead carbonate, and the *substance* crystallised by evaporation of the solution to low bulk and recrystallised from alcohol (yield, 75%); m. p. 225—226°, $[\alpha]_D$ + 114° in water (Found: C, 56·3; H, 6·3; N, 4·7. $C_{14}H_{19}O_6N$ requires C, 56·6; H, 6·4; N, 4·7%).

Oxidation with Periodic Acid.—Periodic acid was determined according to Fleury and Lange (*J. Pharm. Chim.*, 1933, **17**, 107). Sodium metaperiodate was prepared by adding 1 equiv. of sodium hydroxide to the standard periodic acid solution, the final p_H being about 6.

Oxidation of Ethyl N-*Benzoyl Glucosamate by Lead Tetra-acetate.*—327 Mg. of the ester (1 millimol.) were dissolved in 10 ml. of acetic acid which had been distilled over lead tetra-acetate, and 60 ml. of 0·15M-lead tetra-acetate in acetic acid (4·5 millimols.) were added. After 20 mins. at room temperature no tetra-acetate could be detected in the solution. In an experiment on a larger scale where the theoretical amount of the oxidising agent was added slowly, an attempt was made to isolate the products; chloroform extracts, however, gave an uncrystallisable gum having only very weak reducing properties and from which no crystalline derivatives could be obtained. Benzoic acid, hippuric acid and *N*-benzoyl *dl*-serine are stable to lead tetra-acetate under the conditions used.

Oxidation of Ethyl N-*Benzoyl Glucosamate by Periodic Acid.*—4·5 Ml. of 0·5M-periodic acid were added to an aqueous solution of ethyl *N*-benzoyl glucosamate (0·330 g.); the solution turned brown and ammonia was liberated instantly. A titration indicated that all the periodic acid had been taken up. Oxidation with sodium metaperiodate in acetic acid buffer led to similar results. Attempts to isolate the products were unsuccessful. A colour reaction with ferric chloride, described by Erlenmeyer and Stoop (*Annalen*, 1907, **337**, 236) for the compound, was negative.

Oxidation of 3-*Methyl Glucosamic Acid by Periodic Acid.*—2 Ml. of 0·445M-periodic acid were added to 58 mg. of 3-methyl glucosamic acid in water (10 ml.). After 1 hour 1·24 ml. were used up (calc. for three hydroxyl groups, 1·26 ml.). At the same time 1 equiv. of acid was formed. If methyl-red is used as indicator, periodic and iodic acid behave as monobasic acids; an increase in acidity, therefore, must be due to acid formed during the oxidation. 30·2 Mg. of 3-methyl glucosamic acid were treated with 0·9 ml. of 0·445M-periodic acid and left for 2 hours. The solution now required 5·65 ml. of 0·1N-sodium hydroxide, while the same amount of periodic acid uses up 4·20 ml., the difference being 1·45 ml. (calc., 1·44 ml.). The acid was identified as formic acid as follows: 0·5 g. of 3-methyl glucosamic acid was oxidised with the theoretical amount of periodic acid, the iodic acid formed was removed by barium hydroxide, and the neutral solution was evaporated to low bulk. In this distillate the presence of formaldehyde was proved by the formation of its dimedon derivative. The residue was acidified, water added, and the solution again distilled; the second distillate contained an acidic substance reducing silver nitrate. No ammonia or iodine was liberated during the oxidation.

Glucosamic acid, on the other hand, reacts with periodic acid instantly with the appearance of iodine and ammonia in the solution.

Oxidation of N-*Acetyl* α-*Methylglucosaminide by Periodic Acid.*—To a solution of *N*-acetyl α-methylglucosaminide (0·235 g.; 1 millimol.) were added 5 ml. of 0·395M-periodic acid (1·98 millimols.), and the solution made up to 25 ml. The rotation after 24 hours had dropped to zero, the initial $[\alpha]_D$ being + 105°. The oxygen uptake was as follows: 2·5 hrs., 1·13 atoms; 9 hrs., 1·8 atoms; 22 hrs., 1·98 atoms. After 2 hrs. a brown colour appeared in the solution

which increased in intensity as the reaction proceeded. If 1 mol. of periodic acid is added per mol. of substance, 65% of the available oxygen is taken up in 2·5 hrs. Similar results were obtained with *N*-benzoyl α-methylglucosaminide.

If the reaction is carried out at neutral p_H, only one atom of oxygen is taken up and the curves obtained by plotting the changes in rotation and the oxygen uptake against time are identical. This indicates that probably only one primary reaction occurs at neutral p_H. *N*-Acetyl α-methylglucosaminide (0·235 g.) was dissolved in water (25 ml.) containing 5 ml. of 0·422M-periodic acid (2·11 millimols.) and 2·25 ml. of N-sodium hydroxide. Samples were removed at intervals and titrated. The initial oxygen uptake was more rapid than in acid solution, but the oxidation became very slow after one atom of oxygen had been taken up. The figures were as follows: after 1 hour, 0·83 atom; after 3 hrs., 0·99 atom; after 7 hrs., 1·02 atoms; after 17 hrs., 1·06 atoms. The changes in $[\alpha]_D$ were as follows: 1 hour, +48°; 3 hrs., + 33·3°; 7 hrs., + 28·5°; 17 hrs., + 27·9°. The solution remained colourless during the period. Similar results were obtained with the *N*-benzoyl compound.

Attempted Oxidation of N-Acetyl 3-Methyl α-Methylglucosaminide by Periodic Acid.—The α-methylglucosaminide (50 mg.) was dissolved in water (10 ml.) containing 1 ml. of 0·445M-periodic acid. The rotation remained constant during 24 hours, $[\alpha]_D$ being + 114°; no oxygen uptake occurred. Equally negative results were obtained with sodium metaperiodate.

The author wishes to thank Sir F. G. Hopkins for his encouragement. Acknowledgment is also made to the Beit Memorial Trustees for a Fellowship.

BIOCHEMICAL LABORATORY, CAMBRIDGE. [*Received, November 11th*, 1940.]

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13. *The Preparation of 3-Methyl Glucosamine.*

By ALBERT NEUBERGER.

The preparation of 3-methyl glucosamine and 3-methyl glucosamic acid is described and the structure proved by the behaviour of these compounds towards periodic acid.

MANY biologically important carbohydrate derivatives contain amino-sugars and it may be expected that methylation will be, as in non-nitrogenous polysaccharides, a very fruitful method for the elucidation of their structures. It was thought desirable, therefore, to prepare reference compounds, *i.e.*, partially methylated glucosamine and chondrosamine derivatives. As a first step in this work the preparation of *3-methyl glucosamine hydrochloride* is here described.

N-Acetyl α-methylglucosaminide (I) (Moggridge and Neuberger, J., 1938, 745) was condensed with benzaldehyde to give N-*acetyl* 4 : 6-*benzylidene α-methylglucosaminide* (II), the structure of which follows from the reactions of the compounds derived from it. (II) was very sparingly soluble in most solvents and refractory to methylation under the conditions usually applied. N-*Acetyl* 4 : 6-*benzylidene* 3-*methyl α-methylglucosaminide* (III) could, however, be obtained from (II) by using dioxan as a solvent. (III) on hydrolysis with 60% acetic acid gave N-*acetyl* 3-*methyl α-methylglucosaminide* (IV), which on further hydrolysis by 2·5N-hydrochloric acid yielded *3-methyl glucosamine hydrochloride* (V). This compound was oxidised with yellow mercuric oxide to 3-methyl glucosamic acid (VI).

The position of the methyl group proposed for these compounds is proved by the following considerations. Since (I) is a pyranoside (Neuberger, J., 1939, 29), it can be assumed that condensation with benzaldehyde leads, as in other pyranosides, to a 4 : 6-benzylidene compound; the methyl group therefore must enter in position 3. More definite evidence, however, is obtained from the behaviour of (IV) and (VI) towards periodic acid (preceding paper). Periodic acid splits oxidatively carbon–carbon bonds, where either two hydroxyl (Malaprade, *Bull. Soc. chim.*, 1934, **1**, 833) or one hydroxyl and one amino-group (Nicolet and Shinn, *J. Amer. Chem. Soc.*, 1939, **61**, 1615) are attached to two adjacent carbon atoms. In the latter case ammonia is liberated. One atom of oxygen is taken up for each bond split and formic acid is formed if more than two adjacent hydroxyls are present. Now, (IV) is not attacked by periodic acid, indicating that no adjacent hydroxyls are available; this limits the

position of the methyl group to 3 or 4. The behaviour of (VI) to periodic acid, however, excludes the possibility of the methyl group being in position 4. (VI) in the presence of periodic acid takes up two atoms of oxygen, one mol. of formaldehyde and one mol. of formic acid being formed, and no ammonia is liberated. This shows that, first, no free hydroxyl is adjacent to the amino-group and, secondly, all three hydroxyls present in the molecule are adjacent, *i.e.*, positions 4, 5, and 6 must be free.

Experimental.

N-Acetyl 4 : 6-Benzylidene α-Methylglucosaminide.—A mixture of finely ground *N*-acetyl α-methylglucosaminide (7 g.), anhydrous zinc chloride (7 g.), and benzaldehyde (18 ml.) was shaken for 8 hours. The syrup was then poured into water, washed with ligroin, and filtered. The crystalline dried material was recrystallised from methyl alcohol (yield, 85%); m. p. 255°, $[\alpha]_D$ + 19° in chloroform ($c = 0{\cdot}5$, $l = 2{\cdot}0$) (Found : C, 58·6; H, 6·3; N, 4·3. $C_{16}H_{21}O_6N$ requires C, 59·1; H, 6·5; N, 4·3%).

N-Acetyl 4 : 6-Benzylidene 3-Methyl α-Methylglucosaminide.—*N*-Acetyl 4 : 6-benzylidene α-methylglucosaminide (7 g.), dissolved in dioxan (350 ml.), was treated with ten portions of methyl sulphate (30 ml.) and 30% sodium hydroxide solution (66 ml.) at 10-minute intervals at 55°. The mixture was poured into a large volume of water and the crystalline precipitate was filtered off (yield, 90%) and recrystallised from methyl alcohol; m. p. 277—279°, $[\alpha]_D$ + 39° in chloroform ($c = 0{\cdot}52$) (Found : C, 60·2; H, 7·0; N, 4·2; OMe, 18·3. $C_{17}H_{23}O_6N$ requires C, 60·5; H, 6·8; N, 4·2; OMe, 18·4%).

N-Acetyl 3-Methyl α-Methylglucosaminide.—*N*-Acetyl 4 : 6-benzylidene 3-methyl α-methylglucosaminide (0·75 g.) was suspended in 60% acetic acid (15 ml.) and heated on a water-bath; the mixture became clear after 5 mins. and heating was continued for 30 mins. The solution was then evaporated to dryness, and the residue taken up in water, filtered, and evaporated in a vacuum. The crystalline residue was recrystallised from alcohol (yield, 65%); m. p. 211°, $[\alpha]_D$ + 116° in water (Found : C, 47·9; H, 7·5; N, 5·4; OMe, 25·2. $C_{10}H_{19}O_6N$ requires C, 48·2; H, 7·5; N, 5·6; OMe, 24·9%).

3-Methyl Glucosamine Hydrochloride.—*N*-Acetyl 3-methyl α-methylglucosaminide (7·5 g.) was refluxed with 2·5N-hydrochloric acid (100 ml.) for 4 hours. The solution was then treated with charcoal and evaporated to dryness. The solid was dissolved in a small volume of hot methyl alcohol and crystallised by addition of acetone (yield, 75%); m. p. 215° (decomp.). The following changes in specific rotation (in water) were noted : +123° (initial, by extrapolation); +119·5° (3 mins.); +115° (10 mins.); +100° (75 mins.); +91·3° (18 hours) (Found : C, 36·8; H, 6·9; N, 5·9; OMe, 13·4. $C_{17}H_{15}O_5N$,HCl requires C, 36·6; H, 7·0; N, 6·1; OMe, 13·5%).

3-Methyl Glucosamic Acid.—A mixture containing 3-methyl glucosamine hydrochloride (1 g.), dissolved in water (30 ml.), and yellow mercuric oxide (5·5 g.) was heated on a water-bath for 25 mins. and then over a free flame for a further 5 mins. The insoluble material was filtered off, mercury removed by hydrogen sulphide, and the solution evaporated to low bulk. The substance was crystallised by addition of alcohol and recrystallised in the same manner (yield, 70%); m. p. 230° (decomp.), $[\alpha]_D$ − 12° in 5% hydrochloric acid (Found : C, 40·2; H, 7·1; N, 6·7; OMe, 14·0. Calc. for $C_7H_{15}O_6N$: C, 40·2; H, 7·0; N, 6·7; OMe, 13·8%).

Biochemical Laboratory, Cambridge. [*Received, November 11th*, 1940.]

NOTE.

The Elimination of Formaldehyde in the Analysis of Formaldehyde–Formic Acid Mixtures. By A. Hickling and F. Rodwell.

No method appears to have been described for the estimation of formic acid in the presence of excess formaldehyde in solutions containing inorganic acids or alkalis. During an investigation of the electrolytic oxidation of formaldehyde it became necessary to carry out such analyses, and a suitable method has been devised by taking advantage of the almost quantitative precipitation of formaldehyde as trithioformaldehyde by the action of hydrogen sulphide in strongly acid solution (Baumann, *Ber.*, 1890, **23**, 67).

A known volume of the formaldehyde–formic acid solution, which should be free from other oxidisable compounds, is strongly acidified and treated with excess hydrogen sulphide under

defined conditions (see below). The crystalline precipitate of trithioformaldehyde is filtered off, the superfluous hydrogen sulphide in the filtrate removed as copper sulphide, and the excess copper precipitated as oxide by boiling in alkaline solution. The filtrate and washings are then slightly acidified and made up to a known volume. Two equal portions of this solution are taken; in one the small amount of formaldehyde remaining is estimated by oxidation with iodine (Romijn, *Z. anal. Chem.*, 1897, **36**, 19), and in the other the combined formaldehyde + formic acid is determined by oxidation with permanganate in alkaline solution. Both results are obtained in terms of standard sodium thiosulphate solution, and the original concentration of formic acid is then readily calculated.

The following is a typical example of the application of the method. 10 C.c. of a 2M-formaldehyde solution (prepared from paraformaldehyde) containing 0·100M-formic acid were placed in a Winchester-quart bottle, and 20 c.c. of concentrated hydrochloric acid added. The bottle was then filled with hydrogen sulphide and shaken on a mechanical shaker for 3 hours, being twice refilled with gas in this time, after which it was set aside overnight. The contents were then washed through a fritted-glass filter, and 19 c.c. of approximately 10N-sodium hydroxide added to the filtrate, followed by slight excess of copper sulphate (about 3 c.c. of 0·5M-solution). The precipitated copper sulphide was then filtered off, and the filtrate boiled after being rendered alkaline with sodium hydroxide. The copper oxide was removed, and the filtrate and washings were slightly acidified with hydrochloric acid and made up to 250 c.c. The formaldehyde remaining in 100 c.c. of this solution was then estimated by adding 25 c.c. of approx. 0·1N-iodine, followed by 4N-sodium hydroxide until the solution was pale yellow; after standing for 10 minutes, the unused iodine was titrated with 0·100N-sodium thiosulphate. In general, the amount of iodine used was equivalent to 1—2 c.c. of the thiosulphate, showing that less than 1% of the formaldehyde originally present had escaped precipitation by the hydrogen sulphide. Removal of the formaldehyde to this extent seems to be essential; incomplete reaction with hydrogen sulphide appears to lead to other oxidisable substances which are soluble and are ultimately recorded as formic acid. To a second 100 c.c. portion of the solution were added 10 c.c. of 2N-sodium carbonate, followed by 50 c.c. of approximately 0·1N-potassium permanganate, and the mixture heated on a water-bath for 10 minutes. It was then cooled, excess potassium iodide added, the mixture acidified with hydrochloric acid, and the iodine titrated with 0·100N-thiosulphate. If x and y are the amounts of iodine and permanganate used, expressed in terms of the thiosulphate solution, the concentration of formic acid in the original mixture is $[0{\cdot}100(y - 2x)/8]$M. In four consecutive experiments, values of 0·101, 0·101, 0·100, and 0·101M were obtained, in close agreement with the known formic acid concentration. The presence of methyl alcohol in moderate quantity was found not to interfere markedly with the estimation; thus in an experiment in which the solution was made 0·1M with respect to methyl alcohol, the formic acid estimation was only 3% high.—CHEMICAL DEPARTMENT, UNIVERSITY COLLEGE, LEICESTER. [*Received, November 7th*, 1940.]

OBITUARY NOTICES.

SIR HENRY CORT HAROLD CARPENTER.

1875—1940.

SIR HAROLD CARPENTER, Professor of Metallurgy at the Royal School of Mines, died of heart failure on September 13th during a walk in the neighbourhood of Swansea, his department having been transferred there for the duration of the war. Having reached the age of 65 his retirement was due, but he was continuing the work of teaching in the department directed by his former assistant and collaborator, Principal C. A. Edwards, F.R.S.

Carpenter was educated at Eastbourne College, and went to Oxford as a scholar of Merton. Here he gained a first in Natural Science, and in 1898, after graduating Ph.D. at Leipzig, went to Owens College, Manchester, as Research Fellow and Demonstrator in Chemistry. When the National Physical Laboratory was established in 1902 he was chosen to take charge of the work in chemistry and metallurgy. He now turned from organic chemistry to the study of metals, and although the department was a very small one, with little equipment, in the course of three years he carried out several researches of great importance. Chief amongst these was his determination, with B. F. E. Keeling, of the thermal equilibrium diagram of the alloys of iron and carbon. Allowing for the change in the thermometric scale and for the fact that the transformation of iron at about 1400° had not yet been recognised, the accuracy of this determination has been confirmed by the latest work, although in the meantime data from less careful workers had found their way into the text books. The alloys of copper and aluminium were studied in the same accurate way, and other investigations dealt with the heat treatment of high-speed tool steel and with certain complex alloys of iron. Altogether this was a remarkable output for such a young department, and a high standard was set for his successor, Dr. Rosenhain. In 1906 Carpenter was appointed to the chair of Metallurgy in the University of Manchester, and here he built up an important school of research. In 1914, however, he left to occupy the chair at the Royal School of Mines, which had been held by Percy, Roberts-Austen, and Gowland. The School of Mines having been particularly associated with process metallurgy—the smelting of metals—as well as with the metallographic side, Carpenter made a tour of large-scale metallurgical plants in America, with the object of gaining a first-hand acquaintance with the principal processes. His main interest, however, was in the structure and transformations of metallic alloys, and to this aspect of metallurgy his subsequent work was devoted.

While at Manchester, Carpenter's researches dealt mainly with equilibrium diagrams, chiefly of copper alloys, and with changes in solid solutions. At South Kensington he began a series of investigations, largely with the collaboration of Miss C. F. Elam, on the growth of crystal grains on annealing after deformation. This work led to the production of single crystals, first of aluminium and then of other metals, by applying a critical strain, followed by a controlled annealing, a method which proved most fruitful and opened up the field of research on the properties of single crystals of metals, the theoretical importance of which has proved to be immense. These studies, as well as one on the recrystallisation of electro-deposited iron, were illustrated by admirable photographs. Later, he gave much attention to the mode of separation of ferrite and pearlite from austenite during the cooling of steels, and in collaboration with Dr. J. M. Robertson added considerably to the knowledge of this phenomenon, of such industrial importance. Another series of papers dealt with the structure of native metals, and threw light on the processes of their formation.

Carpenter was a successful teacher, and also took a most active part in the organisation of metallurgical science. He was one of the founders of the Institute of Metals, and in due course occupied the presidential chair of that body and also of the Iron and Steel Institute and of the Institution of Mining and Metallurgy. His sound knowledge and courteous manner made him an excellent chairman, and his services to all these bodies were very great. His name is also particularly associated with the report of a Treasury Committee

over which he presided, which was appointed to examine the conditions of professional appointments in the Civil Service, the "Carpenter Report" becoming the basis of the negotiations which continued over some years and resulted in a distinct improvement in the status and salaries of professional civil servants. In his later years he was frequently called on to advise government departments on technical matters.

Just before leaving London for Swansea, Sir Harold Carpenter had completed, in collaboration with Dr. J. M. Robertson, a comprehensive work on metallurgy. "Metals" is unlike any other text book in this field, the two large volumes being a highly readable account of the whole subject, from processes of extraction to the study of crystal structure. Only a very comprehensive knowledge made such a work possible, and the breadth of view shown in its writing is remarkable.

His services to metallurgy and to science in general brought him many honours. He became a Fellow of the Royal Society in 1918 and was knighted in 1929. The Universities of Wales and Sheffield conferred honorary doctorates on him, and he was a corresponding member of the Royal Swedish Academy of Science and an honorary member of the American Institute of Mining and Metallurgical Engineers. He was awarded both the Bessemer and the Carnegie Medal of the Iron and Steel Institute, the Institution of Mining and Metallurgy and the Thomas Turner Gold Medals, the Carl Lueg Gold Medal of the Verein deutscher Eisenhüttenleute, the Platinum Medal of the Institute of Metals, and, only a few months ago, the Honda Gold Medal of the Japanese Institute of Metals.

Carpenter's influence will be greatly missed. He had become the natural leader of the metallurgical profession in this country, and the school which he had formed influenced the development of the subject on the practical as well as on the academic side. His attractive personality played a great part in bringing about that influence, and he had many friends. A lover of the open air and of the mountains, it might have been expected that he would enjoy many years of comparative leisure after his retirement, and his death came as a shock. He is survived by Lady Carpenter, formerly Miss Ethel Lomas, and had no children.

C. H. Desch.

ALEXANDER CHARLES CUMMING.

1880—1940.

Alexander Charles Cumming died suddenly on September 28th, 1940, after a strenuous life, the early part devoted to academic and the later to industrial work.

Born in Melbourne, Victoria, Cumming proceeded from Caulfield Grammar School to the University of Melbourne, where he gained several scholarships and graduated as B.Sc. with First Class Honours in Chemistry in 1902 and as D.Sc. in 1906. At the University he came under the inspiring influence of Professor (later Sir) D. Orme Masson and work upon carbonates, cyanides, cyanates and urea, as well as upon Congo-red and other indicators, was recorded in three contributions to the Society of Chemical Industry, Melbourne, in 1903 and one to the Chemical Society (J., 1903, **83**, 1391).

Awarded an 1851 Exhibition Scholarship in 1904, Cumming came to Dundee, where a life-long association with Professor (later Sir) James Walker began. The latter on his transference to Edinburgh in 1908 invited Cumming to join his staff as a lecturer.

Until he entered chemical industry, Cumming's interests were mainly concerned with analytical and with physical chemistry. In association with S. A. Kay was published "Quantitative Chemical Analysis" in 1913; six editions followed, the latest in 1939. Cumming's "Practical Chemistry for Medical Students" appeared in 1911 and two editions followed. He edited the English version of G. Lunge's classic books—"Sulphuric Acid and Alkali" and "The Technical Chemists' Handbook" and also edited a series of short "Chemical Monographs," the first of which appeared in 1913 and the latest in 1922.

To the Chemical Society he contributed, either alone or in collaboration with students, papers on malacone, zirconium silicate (J., 1908, **93**, 350); estimation of mercury (J., 1913, **103**, 1772), of zinc (*ibid.*, p. 1004), and of potassium (J., 1915, **107**, 361); vapour pressures (J., 1909, **95**, 1772). Other papers included amphoteric electrolytes (*Proc. Roy. Soc.*, 1906,

78, 105), basic copper nitrate (*Proc. Roy. Soc. Edin.*, 1911, **32**, 4), ferric iron reduction (*ibid.*, 1912, **32**, 12), silica plate (*ibid.*, p. 17), electrochemistry of lead (*Trans. Faraday Soc.*, 1907, **2**, 199), strong electrolytes (*ibid.*, p. 213), elimination of potential due to liquid contact (*ibid.*, 1912, **7**, 253), potential due to liquid contact (*ibid.*, 1913, **9**, 174), and Hempel double pipette (*J. Soc. Chem. Ind.*, 1913, **32**, 9).

The course of Cumming's career was entirely altered by the Great War. In a privately printed pamphlet " Starting a War Time Factory," Cumming wrote—" I did not know to whom I should apply, but decided to address a letter to Lord Kitchener, stating I was a trained chemist, that supplies of sulphuric acid and other requirements for making explosives were available in Edinburgh, and asking if my services in this connection would be of any use to the War Office." This letter led to an interview with Lord Moulton and thereafter to the establishment of a " T.N.T." factory in Edinburgh under the directorship of Sir James Walker, A. C. Cumming, and J. W. Romanes in 1915 and subsequently of a Government Factory outside the city in 1916. Only one of the three directors had had previous experience in a chemical factory—J. W. Romanes—and he still carries on the Lothian Chemical Company in Edinburgh, but not for the production of high explosives! The combined efforts of the three led to the production of " T.N.T." of the highest quality and in large quantities. From the Ministry of Munitions of War, Explosives Department, a letter dated November 15th, 1918, to the Manager, H.M. Factory, Craigleith, Edinburgh, contained the following statement with regard to the ultimate destination of nitrogen—" The figures are probably a record for the country and, as happily the war is now over, it does not appear as if they will ever be equalled." H.M. Factory, Craigleith, was immediately closed down and the neighbourhood has become a residential one. In recognition of his services Cumming received the appointment of O.B.E. in 1918.

At the end of the war the University of Edinburgh instituted a Lectureship in Technical Chemistry and Cumming received the appointment. The experience of industrial life during the war tempted him to forsake academic life and in 1921 he went to Liverpool as consultant to Macfie and Sons, Ltd., Sugar Refiners, and three years later he became Managing Director. He reorganised the factory and spent fourteen strenuous years there until its closing in 1938. While in Liverpool he started a small factory for the production of " Klarit," a decolorising carbon.

In recent years Cumming lived at Caldy, Cheshire, or at " Craigness," Glen Isla, Perthshire. He married Miss Blythe Knox of Aberdeen and is survived by her, two sons, and three daughters.

Gifted with much force of character, Cumming was outstanding as a capable and confident teacher, a hard worker, a good organiser, and, to those who knew him well, a constant and sympathetic friend.

He was elected a Fellow of the Chemical Society in 1910, of the Royal Society of Edinburgh in 1914, and of the Institute of Chemistry in 1917.

LEONARD DOBBIN.
JOHN E. MACKENZIE.

SIR ROBERT ABBOTT HADFIELD.

1858—1940.

SIR ROBERT HADFIELD, chairman of the famous steel firm bearing his name, died at his house on Kingston Hill on September 30th, in his 82nd year. Whilst his most important contribution to science was made as far back as 1882, he had throughout his long life occupied a foremost position as an industrialist and as one occupied in the application of science to industry. He was born at Attercliffe, Sheffield, on November 28th, 1858, and was educated at the Collegiate School, Sheffield, where he received some instruction in chemistry. This was encouraged by his father, Robert Hadfield, who was a pioneer in the production of steel castings. At the age of 16 he began work in the firm of Jonas, Meyer, and Colver, and after a few months entered his father's works. Here he was provided with a laboratory, and began the series of experiments which were to prove so fruitful. At

the early age of 24 he was obliged, on account of the elder Hadfield's failing health, to take over the management of the business. The firm was then converted into a limited company, and while continuing the making of steel castings, was widened in scope, specialising also in the production of armaments.

Hadfield's interest in alloy steels was aroused by reading a pamphlet on the alloys of manganese, issued by the Terre Noire Company. It seemed possible that very hard alloys might be obtained if a suitable composition could be found. It was known that, as additions of manganese to steel were increased, the hardness also increased, but from 3% onwards the alloys were too brittle to be of use. Hadfield, however, was not satisfied with this result, and persevered with the investigation, finding that with further additions the brittleness became less, and at 12—13% an alloy was reached having properties which were unlike those of any steel so far obtained. Quenching in water softened instead of hardening it, and the comparatively soft metal became harder under abrasion, giving quite extraordinary resistance to wear. The new alloy, in spite of containing about 86% of iron, was non-magnetic. It proved to be much more important than the very hard alloy which was being sought for, and it soon found its way into engineering practice, being used for crushing machinery, dredger buckets, railway and tramway crossings, and in other situations exposed to severe abrasion. In the war of 1914—18 it found a new and extensive application in the form of the British protective helmets. The discovery was made in 1882, and the first full account of it was given in a paper read to the Institution of Civil Engineers in 1888. The comparative softness and non-magnetic character are now accounted for by the fact that manganese steel belongs to the austenitic class, with the iron retained in the gamma condition, but some of its properties are still anomalous.

Another element which seemed to offer promise of obtaining a hard alloy was silicon, and a systematic study of the influence of successive additions of silicon to iron and steel was made. An improved structural steel was one product of this research, but still more important was the discovery that with 3—4% of silicon, carbon being almost absent, an iron alloy was obtained with high electrical resistance and also very low hysteresis loss. These properties were studied by Sir William Barrett, and the full investigation was described in a paper to the Institution of Electrical Engineers by Barrett, Brown, and Hadfield. This alloy found an important application in the making of transformers, allowing of a great saving in weight. There were difficulties in the making of the steel and in its introduction into industry, so that it was about 21 years after its discovery that the new alloy was produced commercially for electrical purposes.

The plan of investigating systematically the effect of adding progressive quantities of an element to iron or steel, and of determining as many properties as possible of the resulting alloys, was followed by Hadfield in studies of nickel, aluminium, chromium, and tungsten steels. The information thus obtained has proved of value, but no new alloy of outstanding properties resulted.

The direction of a great industrial undertaking came to occupy his time to an ever increasing extent, but Hadfield was an exceptionally hard worker, capable of keeping many lines of work going simultaneously, and his interest in metallurgical investigation never flagged. He was able to interest scientific investigators in the problems of the steel industry, and supplied them with material for the application of such special techniques as they had developed in their own laboratories. A striking example is that of the effect of very low temperatures on metals. Taking advantage of the equipment of the Royal Institution and of the Cryogenic Laboratory at Leyden, he collaborated with Sir James Dewar and later with Prof. Kammerlingh Onnes and with Prof. de Haas in research at temperatures extending even to that of liquid hydrogen. It proved that, whilst most steels become stronger at very low temperatures but lose their ductility, certain alloy steels increase in strength without any loss of ductility, in one instance even with a marked increase. Moreover, a relation between the behaviour of the two classes and their crystal structure was established.

Another investigation dealt with the production of ingots in which the unsound region due to contraction during freezing was reduced to the smallest possible volume in the upper portion. A new method of revealing segregation by pouring molten copper into the mould after it was filled was introduced, and a joint paper with Dr. Burgess of Washington

described practical results in the use of the improvements in casting practice which had been suggested.

The corrosion of iron and steel was a subject on which Hadfield wrote much with the aim of arousing metallurgical opinion on the economic loss sustained from this cause. Apart, however, from the costly stainless steels, no structural steel has yet been obtained which does not owe its resistance to corrosion to the coating of paint or other protective layer which has been applied to it. Experimental work on corrosion by means of exposure tests under service conditions were encouraged by Hadfield, especially in regard to prolonged tests under marine conditions.

He also took a keen interest in the history of iron and steel metallurgy, and besides making a collection of old metallurgical books, examined and described a number of ancient iron objects, including the famous Pillar of Delhi. He obtained permission to make a minute study of the series of alloys of iron prepared by Faraday and preserved at the Royal Institution. A detailed account of this work was published in book form in 1931. Another work, on " Metallurgy and its Influence on Modern Progress," had been published in 1925.

Sir Robert Hadfield was knighted in 1908 and received a baronetcy in 1917. The list of honours which he received was a long one, many institutions at home and abroad having conferred on him honorary membership and awarded him medals. He became F.R.S. in 1909, and joined the Chemical Society in 1916. He was President of the Iron and Steel Institute in 1905—1907 and of the Faraday Society from 1913 until 1920, and members of those bodies will long remember his active interest in their proceedings and his lavish hospitality. He was Master Cutler of Sheffield in 1899—1900, being the second of his family to hold that office, and he was a generous benefactor to the University of Sheffield, taking a keen interest in the work of the metallurgical department. He also gave much consideration to economic questions, and shortly after the last war he proposed and strongly advocated a scheme for an Empire Development Board.

To the outside world he was better known than any other metallurgist, and his striking personality and capacity for making friends, coupled with his incessant activity as a writer and a correspondent, made his circle of acquaintances and colleagues, both at home and abroad, exceptionally wide.

Lady Hadfield, who survives him, was formerly Miss Frances Bett Wickersham, of Philadelphia, and was created C.B.E. in 1918 in recognition of the admirable work which she did in the hospital founded by herself and her husband at Wimereux. During the present war the Hadfield-Spears Ambulance rendered similar services in France.

C. H. Desch.

EDWARD WILLIAM LUCAS.

1864—1940.

Edward William Lucas, whose death occurred suddenly at his house in Ealing on September 16th, 1940, was born at Ashbourne, Derbyshire, in 1864.

He received his general education at Derby Grammar School and after leaving school entered the School of the Pharmaceutical Society, qualifying as a Pharmaceutical Chemist in 1888.

He then entered the services of Messrs. John Bell and Co., Pharmaceutical Chemists of Oxford Street. From 1889 to 1893 he was employed in the Government Laboratory at Hong Kong, and then returned to London to take charge of the laboratory of John Bell and Co. Ten years later he was taken into partnership by the proprietor, Walter Hills, F.C.S., and from this firm sprang two limited companies: John Bell and Croyden, Ltd., of which he was a director for some years, and John Bell, Hills, and Lucas, Ltd., Manufacturing Chemists and Druggists, of which he was co-managing director with J. Stuart Hills till 1930, when he retired from active work, but retained a seat on the Board of Directors.

From 1896 to 1899 he was a member of the Board of Examiners of the Pharmaceutical Society. In 1903 he was elected a Fellow of the Institute of Chemistry and in 1905 a Fellow of the Chemical Society. He was a member of the British Pharmacopœia Reference

Committee and author of " Practical Pharmacy," " The Book of Prescriptions," and joint author of " The Book of Receipts," and " The Book of the Pharmacopœias."

The honour of C.B.E. was conferred upon him in 1918 in recognition of his work in the production of anti-gas respirators in the Great War.

He was a man of wide interests, who had engaged in many hobbies ranging from cycling in his youth to woodworking in his later years. He was also a great reader and possessed a remarkably retentive memory. He was essentially a virile man of action, enthusiastic to a degree upon the latest idea that roused his interest and quick to dismiss it, if it failed to realise his expectation. A very rapid worker, he was possessed of something akin to intuition, which often led him by short-cuts to correct results in chemical and other problems. Though prone to occasional outbursts, he was kind at heart, sympathetic and loyal; indeed a man who held the true affection of all who knew him well.

He leaves a widow, one son and one daughter and many friends to mourn his loss.

J. STUART HILLS.

CHRISTOPHER RAWSON.

1860—1940.

CHRISTOPHER RAWSON, who died in Manchester on May 29th at the age of 80, was elected a Fellow of the Society in 1880. He was one of the few remaining founder members of the Society of Chemical Industry, and one of the two surviving founders of the Society of Dyers and Colourists, of which he was the first Secretary, and of whose *Journal* he was for some years joint editor with Knecht.

Rawson was born in Bradford, one of a family of nine. In 1877 he entered the Royal College of Chemistry, where he studied chemistry under Frankland. After four years as Assistant to the Professor of Chemistry at the Royal Agricultural College, Cirencester, he returned to Bradford, where he later established himself as a consulting chemist.

In 1898 he was invited by the Behar Indigo Planters Association to examine and if possible improve the methods of cultivation and production of indigo in Bengal; the recent introduction of synthetic indigo was already threatening the existence of the natural product. Rawson's reports contained important suggestions for improvements, but he concluded that further efficiency in production must be gained by the application of genetics or by the introduction of varieties of plants with a higher indigotin content. After the Behar planters had decided to discontinue research work, Rawson joined the Badische Anilin und Soda Fabrik and travelled on behalf of this firm in the United States and Persia. In 1912 he was appointed Chief Chemist to the British Cotton and Wool Dyers Association Limited, Manchester, and later became a Director of the Company.

Rawson wrote authoritatively on the manufacture of natural indigo, and the application of the natural and the synthetic product. " A Manual of Dyeing," by Knecht, Rawson, and Loewenthal, was for many years the standard text-book on the subject, and passed through several editions.

Rawson was during his generation one of the best known and most highly respected chemists in the textile industry in the North of England. He had a quiet, gentle manner, and a kindly disposition, a feature of which was his readiness to help younger chemists and to assist in the organisation and improvement of the profession of chemistry—for some time he was Chairman of the Yorkshire Section of the Society of Chemical Industry, and he was one of a number of textile chemists in Manchester whose activities contributed to the founding of the British Association of Chemists. The Worshipful Company of Dyers elected him a Liveryman of the Company.

He was buried at the Southern Cemetery, Manchester, on June 1st, 1940.

F. SCHOLEFIELD.

NORMAN THOMAS MORTIMER WILSMORE.

1868—1940.

NORMAN THOMAS MORTIMER WILSMORE, who retired from the Chair of Chemistry in the University of Western Australia at the end of 1937, died at Claremont, W.A., on June 12th, after a brief illness. He was in his 73rd year.

Wilsmore was born at Williamstown, Victoria, Australia, in 1868. After preliminary schooling, he entered Melbourne University in 1887. He took a science course and graduated in 1890. From this time to 1892 he was engaged in chemical research and consulting work under Professor (later Sir) David Orme Masson. In 1892 he obtained the degree of Master of Science and in 1907 was awarded the D.Sc.

Leaving Australia in 1894, Wilsmore proceeded to University College, London, where for three years he was engaged in research work under Professors William Ramsay and Norman Collie. In 1897 he went to Göttingen primarily to study physical chemistry under Nernst. He also took some special courses in chemistry, physics, and electrical engineering. Four years later he removed to Zurich for the purpose of making a further study of technical chemistry. Shortly after his arrival there he was appointed first assistant in the department of physical and electrochemistry in the Federal Polytechnic under Professor Richard Lorenz. In 1903 he returned to University College, London, as assistant in chemistry. Subsequently he was promoted to be Assistant-Professor. This post he held until the end of 1912, when he left England to take up the Australian appointment. During the period 1903—1912 Wilsmore did valuable work in the teaching of chemistry (particularly physical chemistry) at University College.

In 1911 the University of Western Australia was established by Parliament and in the following year applications were called for the original teaching appointments. Wilsmore was appointed to the Chair of Chemistry. Before he left England, the Chair of Physical Chemistry at Liverpool became vacant in consequence of Professor F. G. Donnan's removal from Liverpool to University College, London, as successor to Sir William Ramsay. The Liverpool Chair was offered to Wilsmore, but he was unable to accept it, as he had already accepted the Australian Chair.

Arriving in Perth, W.A., early in 1913, Wilsmore with other newly-appointed members of the staff commenced the work of drafting regulations and preparing empty rooms to serve the purpose of lecture rooms. The primitive conditions of the Chemistry (and other) Departments improved but slowly, the expected improvements being checked mainly by the War (1914—1918) and financial depression (1931). It was not until near the end of 1935 that permanent Chemistry buildings were opened.

From 1894 to 1897 Wilsmore engaged in research work under Collie and jointly they published an account of the condensation of dehydracetic acid (which Collie at the time was investigating) with naphthalene and *iso*quinoline derivatives. In Göttingen he determined the electrode potentials of 31 metals with reference to the hydrogen electrode as standard. This was published in the *Zeitschrift für physikalische Chemie* and immediately following it was a criticism by Ostwald, who considered the calomel electrode to be preferable. A short time later a joint paper by Wilsmore and Ostwald was published, Wilsmore upholding the hydrogen electrode, especially with acid or alkaline electrolytes, and Ostwald the calomel electrode, the value for which was based on electro-capillarity and so more likely to give a true zero. It must be added that whilst in modern practice the calomel electrode is generally used, the values are usually referred to the hydrogen electrode as recommended by Wilsmore. Wilsmore's work on electrodes was continued after his return to London, where he made improvements in the zinc and cadmium amalgam electrodes. His last paper (1908) on this subject described the determination of electrode potentials in liquid ammonia.

Wilsmore's work on keten was carried out at University College, London. The investigation commenced with the discovery (1907) of keten itself, the simplest member of a group of compounds already known. Two later contributions to the chemistry of keten dealt with its properties, especially its polymerisation to " diketen " and the constitution of this substance. These investigations mark the termination of his original work (1910). It is

particularly interesting to note that keten and diketen have recently become materials of industrial importance.

After his removal to Western Australia Wilsmore found no opportunities for research. Departmental improvements advanced exceedingly slowly. From about 1920 until almost the time of his retirement, laboratory facilities were limited to those necessary for students; and in addition, the necessary literature and time for research were not available. The burden of teaching and administrative work alone was a serious hindrance to laboratory investigation, had that been otherwise possible.

During Wilsmore's tenure of the Chair of Chemistry (1913—1937) he had only one break in University work, *viz.*, during the War, January, 1917, to April, 1919, when he was engaged on important and valuable work in London with the Department of Explosives Supply. His retirement from the Chair took place at the end of 1937 when he reached the age limit. From that time until a few weeks before his death he was engaged privately in research work.

Wilsmore rendered much effective service to scientific organisations in Australia. For a period of several years terminated by his death, he was an active member of the W.A. State Committee of the (Australian) Council for Scientific and Industrial Research. He was twice President of the W.A. State Committee of the Australian Chemical Institute, on the latter of these occasions being also General President of the Council. When the Australian National Research Council was formed, he became an original Fellow and a member of the Executive Committee.

In his relations with his staff, Wilsmore was always friendly and generous. Former students held him in high regard. His standards were high and called for the close attention of those who came under his tuition, from which they received great benefit. After his retirement, students who had graduated in chemistry during his tenure of the Chair provided a fund, the proceeds of which are being used to provide an annual prize, known as the Wilsmore Prize, to be awarded to the most meritorious student of chemistry qualifying for graduation in each Session.

Wilsmore's death occurred after a short illness. He retained his activity practically unimpaired until a month before the end. He leaves a widow and one son.

G. TATTERSALL.

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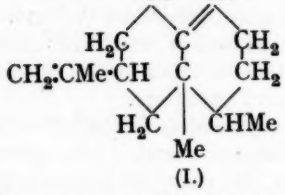
14. *The Constitutions of Eremophilone, Hydroxyeremophilone, and Hydroxydihydroeremophilone. Part IV.*

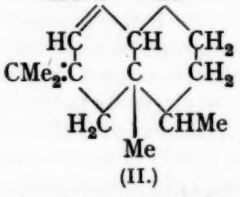
By A. E. GILLAM, J. I. LYNAS-GRAY, A. R. PENFOLD, and J. L. SIMONSEN.

The product resulting from the action of methylmagnesium iodide on hydroxytetrahydroeremophilone methyl ether yields on dehydrogenation with selenium 1 : 6-dimethyl-7-*iso*propylnaphthalene. Structure (V; R = H) is now assigned to hydroxyeremophilone. The representation (I) previously given to eremophilone has been confirmed by the oxidation of this ketone to a tetrabasic acid (XIX). The absorption spectra of hydroxyeremophilone and related ketones have been studied and the results are discussed.

IN Part III (J., 1939, 87) the suggestion was made that eremophilone, hydroxyeremophilone, and hydroxydihydroeremophilone are represented by (I), (II), and (III) respectively. The



(I.)



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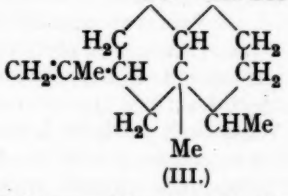


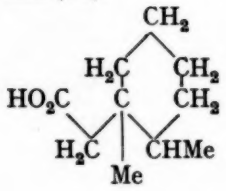
(III.)

recognition of these ketones as derivatives of 1 : 9-dimethyl-7-*iso*propyldecalin has since received support from the synthesis by Copp and Simonsen (J., 1940, 415) of *d*-1 : 2-di-

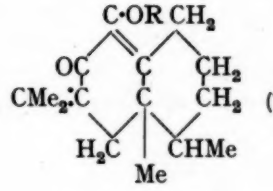
methyl*cyclo*hexylacetic acid (IV), which has been shown to be identical with the *cyclo*hexyl acid derived from hydroxyeremophilone (J., 1938, 773).*

Whilst we can now advance additional evidence in support of the structure (I) assigned to eremophilone, we find (II) and (III) to be incorrect and they should be replaced by (V; R = H) and (VI).

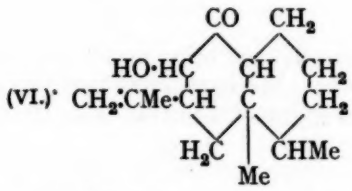
(IV.)



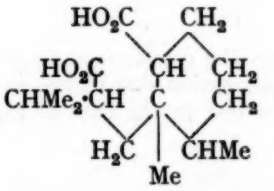
(V.)



(VI.)

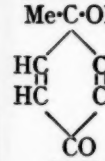


(VII.)



As noted previously (J., 1938, 767), many of the reactions of hydroxyeremophilone suggested that it was a potential 1 : 2-diketone and, since eremophilone oxide can be converted into the hydroxyketone (J., 1932, 2754), one of the carbonyl groups must be in position 5. With the object of establishing rigidly the position of the second (potential) carbonyl group hydroxyeremophilone methyl ether (J., 1938, 771) has been catalytically hydrogenated; the tetrahydro-ether was not obtained pure, but it was characterised by the preparation of its 2 : 4-*dinitrophenylhydrazone*, m. p. 145°. The ketone reacted readily with methylmagnesium iodide and dehydrogenation of the product with selenium gave 1 : 6-dimethyl-7-*iso*propylnaphthalene (J., 1936, 675), which was identified by the preparation of the picrate, m. p. 124—125°, and the styphnate, m. p. 140—141°. It follows, therefore, assuming no molecular rearrangement to occur during the dehydrogenation, that hydroxyeremophilone methyl ether must be represented by (V; R = Me). This structure is in accord with the fact previously recorded (J., 1939, 89) that the glycols prepared from hydroxyeremophilone and hydroxydihydroeremophilone by reduction with sodium and alcohol yield, on oxidation with lead tetra-acetate, followed by potassium permanganate, a dibasic acid, $C_{15}H_{26}O_4$, m. p. 193—194°, which we now consider to be (VII).

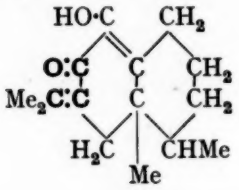
Whilst the structure (V; R = H) undoubtedly represents one of the tautomeric forms of the hydroxy-ketone, the bright yellow colour of the molten ketone and of its solutions suggests that it can exist also as the 1 : 2-diketone, although it has not proved possible to prepare any derivatives of this form. The structure (V; R = H) for hydroxyeremophilone contains a carbonyl group in crossed conjugation with two ethylene linkages. Chromophorically such a system might be expected to absorb similarly to that of a simple cyclic αβ-unsaturated ketone by analogy with three compounds having crossed-conjugated systems quoted by Ruzicka *et al.* (*Helv. Chim. Acta*, 1938, **21**, 1735), namely, $\Delta^{1:4}$-cholestadienone, santonin, and the hydroxy-ketone (VIII). These compounds all exhibit an intense absorption maximum between 2300 and 2420 A. The open-chain example in phorone is apparently exceptional in that the crossed conjugation causes a displacement of the maximum to longer wave-lengths ($\lambda_{max.}$ 2650 A.) as compared with the simple open-chain αβ-unsaturated ketone, mesityl oxide, which is closely similar in absorption spectrum to the cyclic compounds referred to by Ruzicka *et al.* If we tentatively attribute the light absorption of hydroxyeremophilone to the chromophoric properties of a simple αβ-unsaturated ketone only, in the crossed conjugated system we can have either

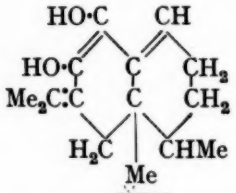


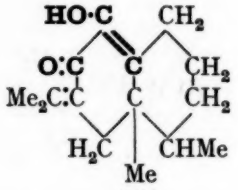
(VIII.)

* The keto-acid, *dl*-6-keto-1 : 2-dimethyl*cyclo*hexylacetic acid, described by Copp and Simonsen, is probably structurally identical with the dextrorotatory keto-acid obtained by the oxidation of hydroxyeremophilone.

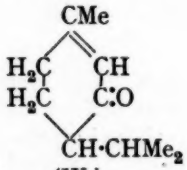
of two chromophoric groups C:C–C:O. Depending upon which of the two ethylene linkages forms part of the effective light-absorbing C:C–C:O group, the chromophore will contain either an *exo*cyclic or a cyclic ethylene linkage (V*a*) or (V*b*). When the ethylene linkage is cyclic, there is the added complication of a hydroxyl group in this particular conjugated system.

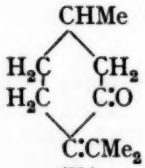

(V*a*.)

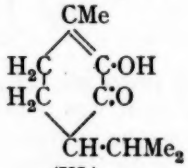

(XII.)


(V*b*.)

This raises the question as to whether the ethylene linkage being cyclic or *exo*cyclic affects the absorption due to the αβ-unsaturated ketone. We have submitted this question to direct test in the case of piperitone (IX) and pulegone (X) (Fig. 1). It will be


(IX.)

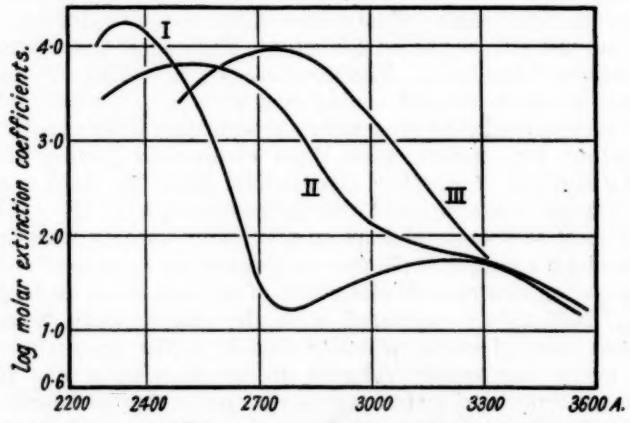

(X.)


(XI.)

seen that, whilst the low-intensity absorption band due to the carbonyl group is unaltered in the two cases, the high-intensity band due to the conjugated system is displaced from 2355 A. in piperitone to 2520 A. in pulegone, the displacement being presumably due to the change from a cyclic to an *exo*cyclic ethylene linkage. To complete the analogy, diosphenol (XI), which is identical with piperitone except that there is a hydroxyl group on one of the two carbon atoms in the ethylene linkage, has also been examined. It will be seen that the presence of the hydroxyl group causes a displacement of the ethylene band to longer wave-lengths (2355 to 2740 A.) and the disappearance (or masking) of the absorption band due to the carbonyl group. This property of the hydroxyl group in modifying

FIG. 1.

The effect of molecular environment on the absorption due to the C=C—C=O *chromophore.*



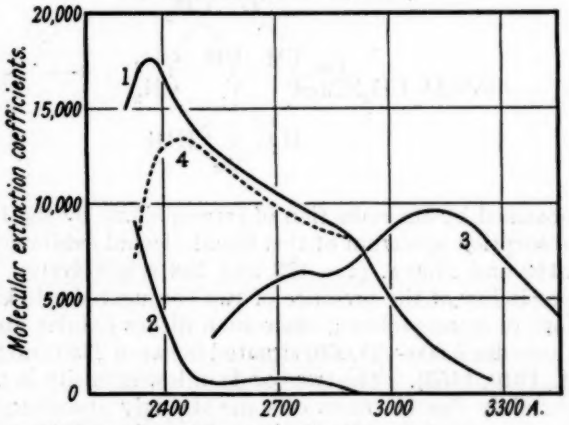
I *Piperitone.* II *Pulegone.* III *Diosphenol* (*solutions in alcohol*).

the absorption spectrum of αβ-unsaturated ketones is also shown in hydroxymethylene-camphor (Fig. 4), where the normal ethylene band is displaced to longer wave-lengths

(*i.e.*, from *ca.* 2350 A. to 2645 A.). Other diosphenols showing the same effect have been recorded: Butenandt *et al.* (*Ber.*, 1936, **69**, 2779) found cholestane-3 : 4-dione-enol to absorb maximally at 2800 A. and Stiller and Rosenheim (J. 1938, 353) found that cholestane-2 : 3-dione exists in two enolic forms absorbing at 2720 (log $\varepsilon = 3{\cdot}70$) and 2700 (log $\varepsilon = 3{\cdot}93$). Heywood and Kon (J., 1940, 713) also have drawn attention to several cases of enolised diketones showing absorption maxima between 2640 and 2745 A. Thus the location to be expected for hydroxyeremophilone would be very similar to that of diosphenol, *i.e.*, 2740 A. In actual fact the main maximum is situated at 3125 A. with a subsidiary inflection at 2775 A. (Fig. 2). To explain this location necessitates a formula containing a longer chain of ethylene linkages and the most probable way to obtain this is to postulate a tautomerism of (V*a*) to (XII) in alcoholic solution.

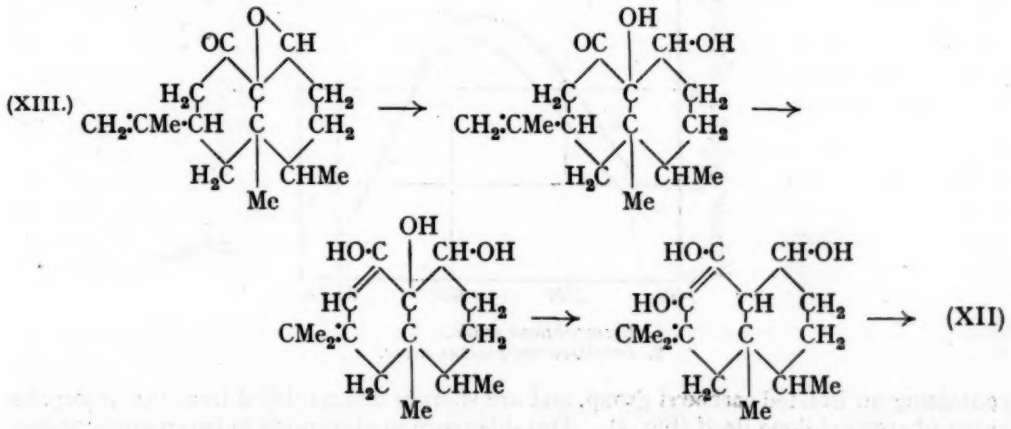
FIG. 2.

Absorption spectra in ethyl alcohol.



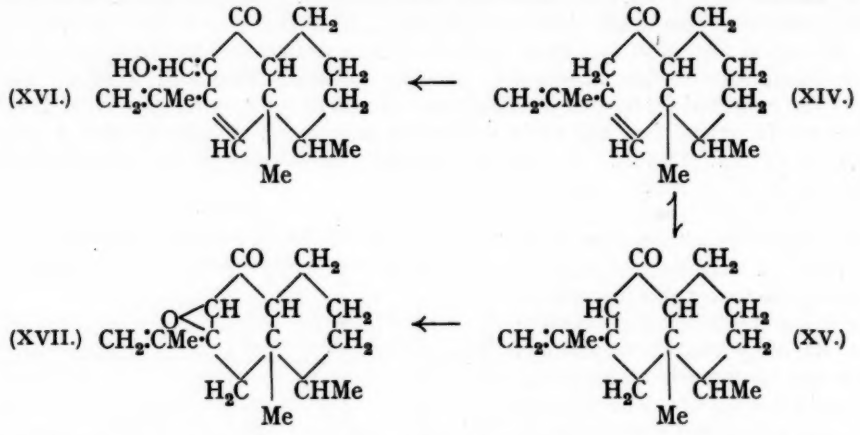
1. *Hydroxyeremophilone benzoate (observed).*
2. *Benzoic acid (observed).*
3. *Hydroxyeremophilone (observed).*
4. *Hydroxyeremophilone as present in the benzoate (by difference, curve 1 minus curve 2).*

It is possible to test this hypothesis by examining the benzoyl derivative (V; R = Bz) of hydroxyeremophilone, in which the tautomeric change suggested could not occur. The absorption spectra concerned are shown in Fig. 2, where it will be seen that, after allowing for the absorption of the benzoate radical, the absorption of hydroxyeremophilone in the combined state is quite different from that of the free compound. The displacement to longer wave-lengths in the case of the free compound is consistent with an increase of the conjugated system such as is indicated in the postulated tautomeric form (XII). It was difficult at first to reconcile the constitution now assigned to hydroxyeremophilone with its formation from eremophilone oxide, which, if (I) correctly represents eremophilone, must be (XIII). We now venture to suggest that the mechanism of this reaction is that outlined in the scheme set out below, which involves an anionotropic rearrangement.



Before this mechanism was evolved it appeared to us possible that eremophilone might be an equilibrium mixture of (XIV) and (XV); hydroxymethylene-eremophilone (XVI) would then be derived from (XIV), and the oxide (XVII) from (XV). Although indirect

evidence was already available (J., 1938, 771) that the ethylene linkages in eremophilone were not conjugated, it was desirable to obtain further confirmation. This has now been

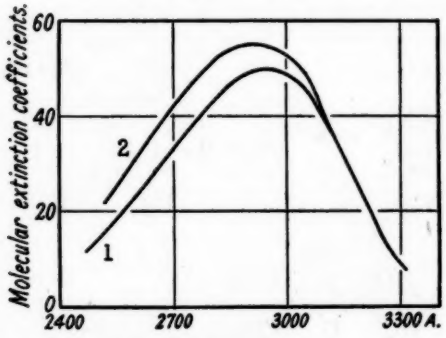


obtained by the reduction of eremophilone by the Ponndorff method to *eremophilol*. The absorption spectrum of this liquid alcohol exhibited two maxima of very low intensity at 2440 and 2750 A. ($\varepsilon = 193$ and 188 respectively). This result completely rules out the possibility of the presence of two conjugated ethylene linkages in eremophilol (and therefore in eremophilone), since such dienes exhibit absorption bands of high intensity (ε of the order 5,000—35,000) situated between 2350 and 2650 A. (cf. Booker, Evans, and Gillam, J., 1940, 1453). The two bands of low intensity in the specimen of eremophilol are almost certainly due to traces of some strongly absorbing impurities in the oil, which had only been purified by distillation. Less than 2% of compounds containing C : C–C : C or C : C–C : O groups would be sufficient to account for the observed intensity, although only the 2440 A. band could be due to the most likely impurity, eremophilone.

The absorption spectra of eremophilone oxide and of dihydroeremophilone oxide are shown in Fig. 3, the curves being typical, in both location and intensity, of compounds

FIG. 3.

Absorption spectra in ethyl alcohol.



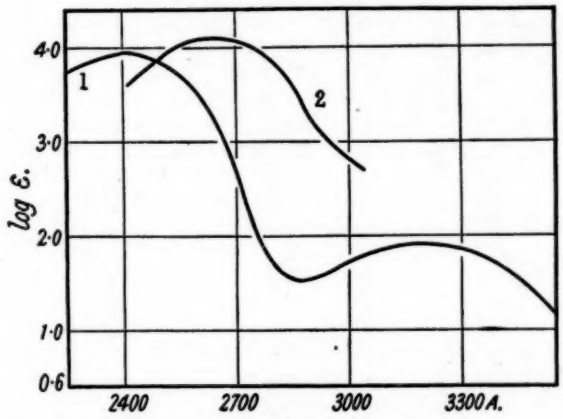
1. *Eremophilone oxide.*
2. *Dihydroeremophilone oxide.*

containing an isolated carbonyl group, and are sharply differentiated from the absorption curve of eremophilone itself (Fig. 4). This difference in absorption between eremophilone and eremophilone oxide is sufficient in itself to indicate that the oxygen atom in the oxide has attached itself to the ethylene linkage originally in conjugation with the carbonyl group.

Although there was already available proof that eremophilone contained an *iso*propenyl side chain, the position of the second ethylene linkage had not been directly determined.

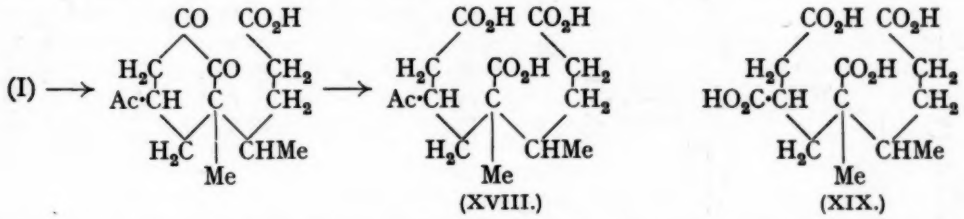
FIG. 4.

Absorption spectra in ethyl alcohol.



1. *Eremophilone (typical of most αβ-unsaturated ketones).*
2. *Hydroxymethylenecamphor (a typical hydroxylated αβ-unsaturated ketone).*

We have now oxidised eremophilone with ozone and have obtained as the main product of the ozonolysis (apart from formaldehyde) a polybasic keto-acid. On the basis of (I) the keto-acid would be (XVIII); neither the acid nor its methyl ester was obtained pure,



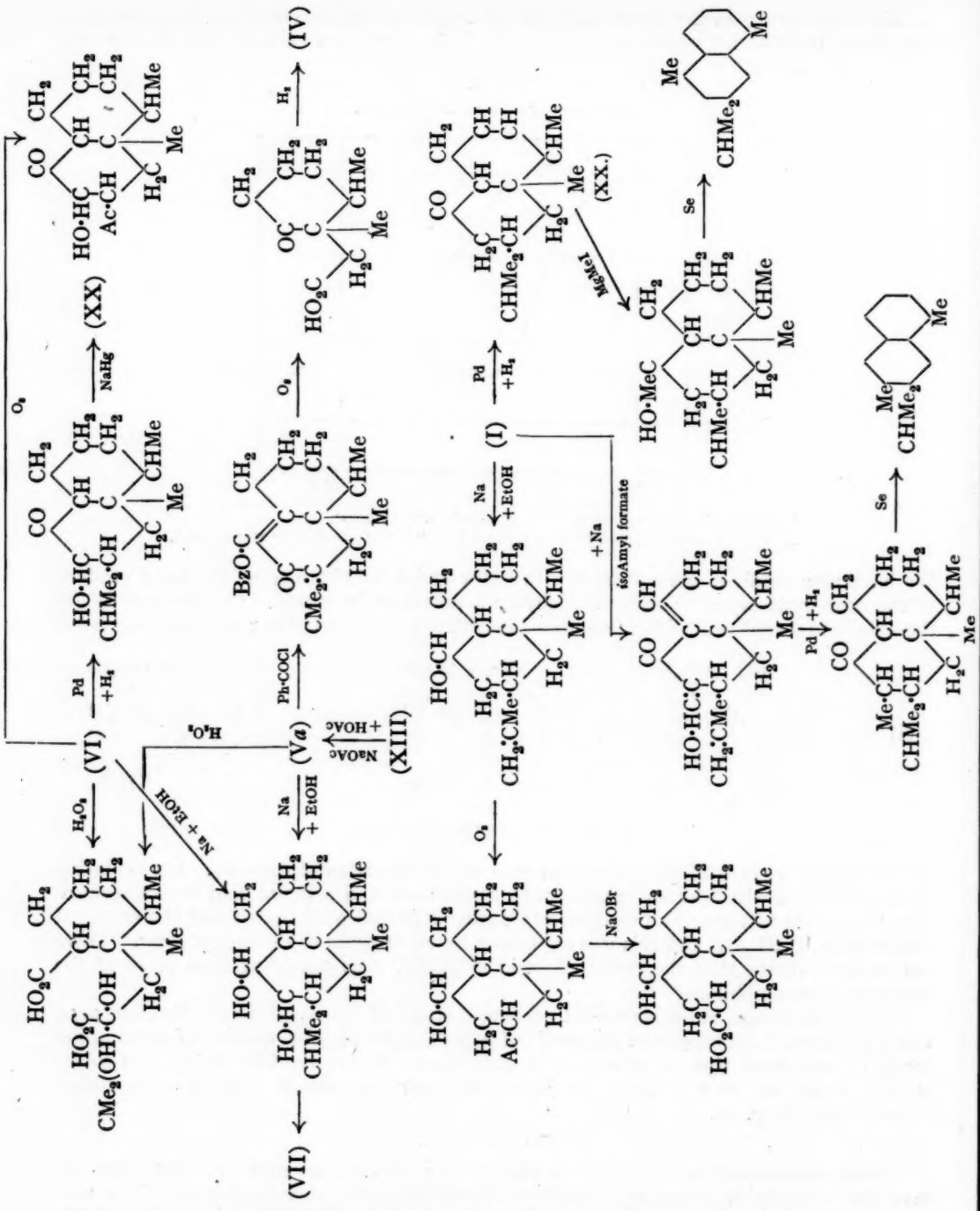
(XVIII.) (XIX.)

nor did they give crystalline derivatives with the usual carbonyl reagents. On oxidation of the keto-acid with sodium hypobromite, bromoform and a liquid acid were obtained. Titration of the latter and an analysis of its *silver* salt indicated that it had the expected composition, $C_{13}H_{20}O_8$, and this was confirmed by an analysis of the *methyl* ester. There can be little doubt that the tetrabasic acid is (XIX), thus providing final proof of the structure of eremophilone.

During the course of the somewhat prolonged study of eremophilone and its congeners, which has formed the subject of this series of papers, a considerable number of degradation products have from time to time been described and incorrectly formulated. In so far as they have not been referred to above the more important reactions are shown schematically on p. 66.

EXPERIMENTAL.

Tetrabromoeremophilone.—Contrary to the results previously recorded (J., 1932, 2752) we have now succeeded in preparing a crystalline bromo-derivative of eremophilone. To a well-cooled solution of the ketone (0·5 g.) in chloroform (5 c.c.) a chloroform solution of bromine (1 c.c. equiv. to 1 g. of bromine) was slowly added. Bromination was complete after the addition of 0·8 c.c. and removal of the solvent under diminished pressure gave an oil from which hydrogen bromide was slowly evolved. On trituration with ligroin (b. p. 40—60°) a solid separated. *Tetrabromoeremophilone* was best purified by solution in cold benzene and precipitation by careful addition of ligroin; it then formed highly iridescent prisms, decomp. 116°



(Found: Br, 59·0. $C_{15}H_{22}OBr_4$ requires Br, 59·5%). The tetrabromide was somewhat unstable and decomposed if its solution in alcohol or ethyl acetate was warmed.

Eremophilol.—A mixture of eremophilone (10 g.), *iso*propyl alcohol (50 g.), and aluminium *iso*propoxide (3·5 g.) was distilled with an efficient column until acetone could no longer be detected in the distillate; during the distillation the volume was kept constant by the addition of *iso*propyl alcohol. The excess of *iso*propyl alcohol was removed by distillation, the cooled

residue mixed with dilute sulphuric acid, and the oil which separated dissolved in ether. The dried ethereal extract gave on evaporation an oil (7·5 g.). *Eremophilol*, b. p. 164—165°/13 mm., n_D 1·5202, $[\alpha]_{5461}$ − 55·6° in methyl alcohol (*c*, 5·25) (Found: C, 81·6; H, 10·8. $C_{15}H_{24}O$ requires C, 81·8; H, 10·9%), was a somewhat viscid oil with a pleasant odour. The 3 : 5-*dinitrobenzoate*, prepared by treating the oil with 3 : 5-dinitrobenzoyl chloride in pyridine solution, was a gum which partly crystallised on trituration with methyl alcohol. The solid (2 g. from 5 g. of the alcohol) separated from methyl alcohol in needles, m. p. 88—89°, $[\alpha]_{5461}$ − 149·4° in ethyl acetate (*c*, 0·813) (Found: C, 63·6; H, 6·4. $C_{22}H_{26}O_6N_2$ requires C, 63·8; H, 6·3%).

Ozonolysis of Eremophilone.—Eremophilone (10 c.c.) in methyl acetate (50 c.c.) was ozonised at 0°. Formaldehyde was present in the issuing gases, but only a trace of acetone could be detected on decomposition of the ozonide. After completion of the ozonolysis the solvent was removed under diminished pressure, water (10 c.c.) added, and the resinous ozonide decomposed by heating on the water-bath. Addition of sodium carbonate to the aqueous solution left a neutral oil (1·6 g.) undissolved; this was removed by ether, the alkaline solution acidified, and the liquid keto-acid extracted with ether. Evaporation of the solvent from the dried extract gave a viscid oil (12 g.), which reacted rapidly with the ordinary carbonyl reagents, but the products were amorphous. The *methyl* ester, prepared by means of diazomethane, was a somewhat viscid, yellow oil, b. p. *ca.* 220°/18 mm., analysis showing it to be impure (Found: C, 60·7; H, 8·3. $C_{17}H_{28}O_7$ requires C, 59·3; H, 8·1%). For conversion into the tetracarboxylic acid, the keto-acid (12 g.) in aqueous sodium hydroxide was oxidised with aqueous sodium hypobromite (sodium hydroxide, 21 g.; water, 280 c.c.; bromine, 22·8 g.). Bromoform separated immediately and after 1 hour this was removed, the excess of sodium hypobromite destroyed with sulphur dioxide, and the tetra-basic acid extracted by ether from the acidified solution in a constant-extraction apparatus. The acid (12 g.) was a gum which on titration showed the presence of only three carboxyl groups (Found: *M*, 310. $C_{13}H_{20}O_8$ requires *M*, 304), and this was confirmed by the analysis of the *silver* salt (Found: Ag, 51·3. $C_{13}H_{17}O_8Ag_3$ requires Ag, 51·8%). The acid was esterified with diazomethane in ethereal solution, the *methyl* ester being an oil, b. p. 203—205°/5 mm., $[\alpha]_{5461}$ − 17·5° in methyl alcohol (*c*, 6·03) [Found: C, 56·4; H, 7·3; OMe, 41·3, 41·6. $C_{13}H_{16}O_4(OMe)_4$ requires C, 56·7; H, 7·8; OMe, 34·4%. The high methoxyl value is due probably to the partial elimination of the angle methyl group].

Conversion of Hydroxyeremophilone Methyl Ether into 1 : 6-*Dimethyl*-7-iso*propylnaphthalene.*—A solution of hydroxyeremophilone methyl ether (20 g.) in alcohol (100 c.c.) containing palladium–norit (1 g.; 10%) was shaken with hydrogen, absorption corresponding to approximately 2 molecules being complete in 15 hours. The resulting oil, b. p. 175—176°/19 mm., $d_{19\cdot8°}^{19\cdot8°}$ 0·9989, $n_D^{19\cdot8°}$ 1·5045, $[\alpha]_{5461}$ + 47·9°, gave with alcoholic ferric chloride an intense blue colour, indicating that the hydrogenation had been accompanied by some hydrolysis [Found: C, 77·9; H, 10·6; OMe, 13·1. $C_{15}H_{25}(OMe)$ requires C, 76·2; H, 11·1; OMe, 12·3%]. The oil gave a gummy 2 : 4-dinitrophenylhydrazone. It was remethylated and on hydrogenation the methyl ether (12 g.) absorbed hydrogen (600 c.c.). The product, which now gave only a faint colour with ferric chloride, had b. p. 168°/16 mm., $d_{19\cdot8°}^{19\cdot8°}$ 0·9983, $n_D^{19\cdot8°}$ 1·4848, $[\alpha]_{5461}$ + 17·2°, and was still impure (Found: 79·1; H, 10·6%). It gave, however, a crystalline 2 : 4-*dinitrophenylhydrazone*, separating from alcohol in fine yellow needles, m. p. 140° (Found: C, 61·0; H, 7·3. $C_{22}H_{32}O_5N_4$ requires C, 61·1; H, 7·4%).

The methyl ether (10 g.) in ether (500 c.c.) was added to an ethereal solution of methylmagnesium iodide (from 2 g. of magnesium). Interaction was vigorous and, after being kept overnight, the mixture was heated on the water-bath for ½ hour. Isolation of the product in the usual manner gave an oil (9·5 g.), b. p. 148—160°/16 mm., which did not react with Brady's reagent. The oil (5 g.) was heated with selenium (5 g.) at 270° for 12 hours and for a further 36 hours at 300—320°. The product was dissolved in ether, the ethereal extract washed with aqueous sodium hydroxide and water, and the solvent removed from the dried extract. The residual oil (2 g.) was distilled over sodium, b. p. 150—152°/14 mm. From the distillate the picrate was prepared, which crystallised from alcohol in orange-red needles, m. p. 124—125°, and at 124—126° in admixture with the picrate of 1 : 6-dimethyl-7-*iso*propylnaphthalene (Found: C, 59·1; H, 4·8. Calc. for $C_{15}H_{18}.C_6H_3O_7N_3$: C, 59·0; H, 4·9%). The styphnate crystallised from alcohol in fine yellow needles, m. p. 140—141°, both alone and in admixture with 1 : 6-dimethyl-7-*iso*propylnaphthalene styphnate (Found: C, 57·4; H, 4·9. Calc. for $C_{15}H_{18}.C_6H_3O_8N_3$: C, 56·9; H, 4·7%).

Absorption Spectra.—The determinations were made by standard methods, a Hilger E3 spectrograph being used with a Spekker photometer; unless otherwise stated, purified ethyl alcohol was the solvent.

Piperitone. This was obtained from a commercial specimen and was purified by conversion into its semicarbazone, from which it was regenerated by hydrolysis with oxalic acid. It exhibited an absorption spectrum of the most characteristic αβ-unsaturated ketone-type, the ketone band being exceptionally well defined and of good persistence (Fig. 1). The maxima were situated at 2355 and 3210 A., the values of ε being 17,780 and 54 respectively.

Diosphenol. The absorption spectrum of this compound has been determined by a semi-quantitative method (Mayer, *Atti R. Accad. Lincei*, 1914, **23**, *I*, 439), $\lambda_{max.}$ 2680 A. being recorded. Walker and Read (J., 1934, 230) record $\lambda_{max.}$ 2715 A., $\varepsilon = 11{,}000$, but give no absorption curve. We are indebted to Professor Read for a specimen of diosphenol, for which we have found $\lambda_{max.} = 2740$ A., $\varepsilon = 11{,}000$ (Fig. 1).

Pulegone. Our thanks are due to Professor A. R. Todd and Mr. D. C. Wright for a pure specimen of this compound, prepared from oil of pennyroyal *via* the bisulphite compound and the semicarbazone. The product was free from *iso*pulegone. Absorption data have been recorded by Lowry, Simpson, and Allsopp (*Proc. Roy. Soc.*, 1937, *A*, **163**, 486) for *cyclo*hexane solution and by Savard (*Bull. Soc. chim.*, 1928, **43**, 524) for hexane solution. For alcoholic solution we have found $\lambda_{max.}$ 2520 A., $\varepsilon = 6500$ for the ethylene band and only an inflexion of negligible persistence for the >CO group ($\lambda_{max.}$ *ca.* 3250 A., $\varepsilon = 63$).

We are indebted to Imperial Chemical Industries Ltd. for a grant, and one of us (J. I. L.-G.) has been in receipt of a maintenance grant from the Department of Scientific and Industrial Research.

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THE TECHNOLOGICAL MUSEUM, SYDNEY, N.S.W. [*Received, November 15th*, 1940.]

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15. *The Synthesis of* 1-*Methyl*-6-iso*propylphenanthrene.*

By S. N. SLATER.

The synthesis of 1-*methyl*-6-iso*propylphenanthrene* by the Cook–Bogert method is described. It is shown to be different from the hydrocarbon obtained by dehydrogenating the diterpene rimuene.

IN 1904 Easterfield and Bagley (J., 1904, **85**, 1238) isolated a hydrocarbon $C_{18}H_{18}$, m. p. 86°, from the dehydrogenation product of abietene, and Beath (*J. Soc. Chem. Ind.*, 1933, **52**, 338T) later isolated from the dehydrogenation products of the diterpene rimuene a hydrocarbon $C_{18}H_{18}$, m. p. 86—87° (picrate, m. p. 127°, giving a definite depression with authentic retene picrate, m. p. 127°). The similarity in m. p. and analytical figures between this hydrocarbon and that obtained by Easterfield and Bagley (to which the name *iso*retene had been given) suggested that the two might in fact be identical and Beath reported that a mixed m. p. determination (85—86°) confirmed this view. The structure 1-methyl-6-*iso*propylphenanthrene was proposed for *iso*retene, although there was little or no positive evidence to support this formula.

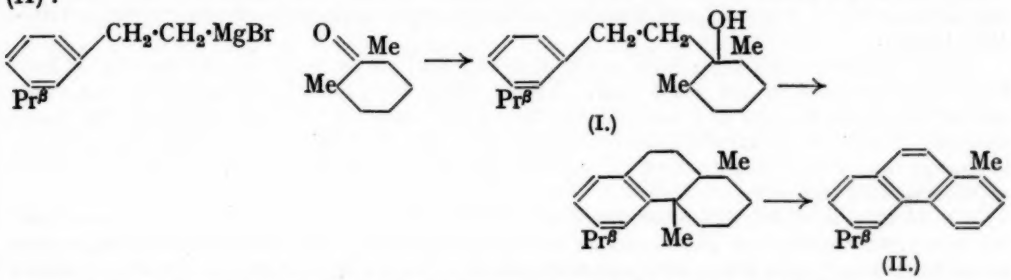
Hosking and McFadyen (*J. Soc. Chem. Ind.*, 1934, **53**, 195T) showed, however, that Easterfield and Bagley's hydrocarbon was almost certainly pimanthrene (1 : 7-dimethylphenanthrene, m. p. 86°; picrate, m. p. 131°) derived from the dehydrogenation of varying amounts of pimarene normally present in abietene. On this view Beath's dehydrogenation product from rimuene would also be identified with pimanthrene.

In confirmation of this Brandt (*N. Z. J. Sci. Tech.*, 1938, **20**, No. 1, 8*B*) subjected a sample of Beath's rimuene to selenium dehydrogenation and isolated a hydrocarbon, m. p. 86°, (50—60% yield) identified as pimanthrene by means of the picrate, styphnate, and quinone.

That Beath's original suggestion was erroneous is further proved by the synthesis of 1-*methyl*-6-iso*propylphenanthrene* described below. The hydrocarbon melted at 45—46°, the *picrate* at 143°, and the *quinone* at 144—146°.

Under conditions similar to those described by Sterling and Bogert (*J. Org. Chem.*, 1939, **4**, 26) the Grignard reagent from homocuminyl bromide (Simonsen and co-workers, J., 1936, 674) was condensed with 2 : 6-dimethyl*cyclo*hexanone (Ruzicka and co-workers,

Helv. Chim. Acta, 1931, **14**, 1163), and the resulting *carbinol* (I) cyclodehydrated with sulphuric acid and dehydrogenated with selenium to 1-methyl-6-*iso*propylphenanthrene (II) :



A related problem is the dehydrogenation of phyllocladene, a diterpene which was shown by Briggs (J., 1937, 79) to be identical with the diterpenes dacrene and sciadopitene. Both rimuene and phyllocladene may be isomerised to the same substance, *iso*phyllocladene.

Uota (*J. Dept. Agr. Kyushu Imp. University*, 1937, **5**, 117) has studied the selenium dehydrogenation of phyllocladene (sciadopitene) and obtained a hydrocarbon (scianthrene), m. p. 86°. The m. p.'s of its derivatives are fairly close to those of retene, but Uota states that the hydrocarbon is distinct from retene and assigns it the structure 7-methyl-1-*iso*propylphenanthrene. Brandt, however (*loc. cit.*), has disputed this interpretation and states that the dehydrogenation of phyllocladene yields a mixture of substances, separated with difficulty into pimanthrene, retene, and two other hydrocarbons, one liquid and one crystalline, the last two being obtained in amounts too small for purification. It is suggested that scianthrene may be a mixture of retene and pimanthrene.

The liquid hydrocarbon obtained by Brandt in small amount gives a picrate, m. p. approx. 144°, and it would be of interest to compare this with the picrate of 1-methyl-6-*iso*propylphenanthrene. The latter hydrocarbon is difficult to crystallise unless pure.

Experimental.

Ethyl p-iso*Propylphenylacetate*.—*p-iso*Propylphenylacetonitrile (43 g.) (Baker, Dippy, and Page, J., 1937, 1777), ethyl alcohol (60 g.), and sulphuric acid (24 g.) were refluxed at 130° for 8 hours. The excess of alcohol was then distilled off, water added, and the ester taken up in ether, filtered from the amide formed, dried over anhydrous sodium sulphate, and distilled; b. p. mainly 135°/12 mm. Yield, 30 g.

β-p-iso*Propylphenylethyl Alcohol* (*Homocuminyl Alcohol*).—A solution of the preceding ester (38 g.) in well-dried ethyl alcohol (200 g.) was added to sodium (18 g.) at 180°. When the vigour of the reaction abated, heating was continued at 160°. From time to time additions of absolute alcohol and of alcohol containing increasingly large quantities of water were made while the temperature was allowed to fall to 100°. Most of the alcohol was then steam-distilled and the residual oil was taken up in ether, washed with dilute acid and with potassium bicarbonate solution, dried over anhydrous sodium sulphate, and distilled; b. p. 127—129°/11 mm. Yield, 17 g.

The carbinol was converted as described by Simonsen and co-workers (J., 1936, 674) into the bromide, b. p. 134—135°/17 mm.

2 : 6-*Dimethyl*-1-β-p-*cuminylethyl*cyclo*hexanol* (I).—The Grignard reagent prepared from homocuminyl bromide (18 g.), ether (2 vols.), and magnesium (1·9 g.) activated with iodine was cooled in a freezing-mixture, and 2 : 6-dimethyl*cyclo*hexanone (8 g.) in ether (1 vol.) dropped in with stirring. After standing in the freezing mixture for 2 hours and then at room temperature overnight, the product was decomposed with ice-cold dilute sulphuric acid, and the ethereal solution washed with sodium bicarbonate solution, dried over anhydrous sodium sulphate, and distilled. The yield of the *carbinol*, b. p. 164—172°/0·5 mm., was 8 g. (Found for a portion, b. p. 165°/0·5 mm. : C, 84·1; H, 10·9. $C_{19}H_{30}O$ requires C, 83·2; H, 10·9%).

1 : 12-*Dimethyl*-6-iso*propyl*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene*.—The carbinol (8 g.) was added slowly to a stirred well-cooled mixture of sulphuric acid (17 g.) and water (3 c.c.). The product was allowed to reach room temperature and then washed into a separating funnel

with light petroleum (b. p. 60—80°; 30 c.c.) and shaken with several portions of 85% sulphuric acid until the acid layer was almost colourless. The petroleum layer, possessing a slight fluorescence, was washed with potassium carbonate solution, then with water, dried over anhydrous sodium sulphate, and distilled, yielding a clear colourless oil (6·2 g.), b. p. 180—190°/12 mm.

1-*Methyl*-6-iso*propylphenanthrene*.—The above oil (6 g.) was heated with selenium (5 g.) at 300° for 6 hours and then at 340° for 1 hour. After cooling, the product was extracted with ether and distilled over sodium in a vacuum, yielding a viscous oil (4·2 g.) with a strong lilac fluorescence. This was converted by alcoholic picric acid (5 g.) into the *picrate*, which was obtained in orange microcrystalline needles, m. p. 143° (Found: C, 62·2; H, 4·5. $C_{18}H_{18},C_6H_3O_7N_3$ requires C, 62·2; H, 4·5%).*

The picrate, in ether, was decomposed by shaking with successive portions of concentrated aqueous ammonia until the yellow colour was completely removed. The ethereal solution was washed with dilute acid, with water, and with sodium bicarbonate solution, dried over anhydrous sodium sulphate, and distilled over sodium in a vacuum, yielding a fluorescent oil (2 g.). On cooling in a freezing mixture this solidified. 1-*Methyl*-6-iso*propylphenanthrene* crystallised from alcohol in masses of small plates, m. p. 45—46° (Found: C, 92·4; H, 7·6. $C_{18}H_{18}$ requires C, 92·3; H, 7·7%).*

The *quinone* was prepared by slowly adding a solution of chromic acid (0·5 g.) in acetic acid (0·8 c.c.) and water (0·4 c.c.) to the hydrocarbon (0·2 g.) in acetic acid (1 c.c.) at 60—70°. After being heated on the water-bath for 1 hour, the product was cooled and diluted with water; the precipitated quinone crystallised from alcohol in fine needles, m. p. 144—146° (Found: C, 81·9; H, 6·1. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%).*

My thanks are due to the University of New Zealand for the award of a Post Graduate Scholarship in Science.

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16. *Further Experiments on the Oxidation of Alkyl Tellurides.*

By Michael P. Balfe and Kamada N. Nandi.

Three amorphous insoluble oxidation products of high melting point have been obtained by the action of air or of hydrogen peroxide on di-*n*-amyl telluride and the ethyl and *l*-menthyl esters of *n*-amyltelluroacetic acid. They are n-*amyltellurinic acid*, $C_5H_{11}\cdot TeO\cdot OH$, a substance, $C_5H_{11}\cdot TeO\cdot CH_2\cdot CO_2Et,2C_5H_{11}\cdot TeO_2H$, and a *substance*, $3(C_5H_{11})_2TeO,C_5H_{11}\cdot TeO_2H$. Derivatives of quadrivalent tellurium obtained from the above three alkyl tellurides are freely soluble and of low melting point.

These observations are similar to those made by Balfe, Chaplin, and Phillips (J., 1938, 341) in experiments with other alkyl tellurides.

Balfe, Chaplin, and Phillips (J., 1938, 342), from an investigation on the oxidation of di-*n*-butyl telluride and other alkyl tellurides, suggested that the telluroxides which are the initial products of the oxidation are unstable and are rapidly converted into *n*-butyltellurinic acid, which is not a simple substance, but exists only as a complex polymeride. In some cases, telluroxide molecules may be incorporated in this polymeride and so become stabilised. This suggestion has not subsequently been controverted, and the properties of the substance described as the anhydride of methyltellurinic acid (Drew, J., 1929, 560), which, from the analytical figures given, may have been a similar complex, and the properties of certain substances described by Bird and Challenger (J., 1939, 163) are in harmony with it. The present experiments, on di-*n*-amyl telluride and certain of its derivatives, were undertaken to test and, if possible, to extend, the previous suggestions. The greater instability of the present compounds restricted the work and it can, therefore, only be said that the results obtained are in agreement with the suggestions made by Balfe, Chaplin, and Phillips (*loc. cit.*).

n-*Amyltellurinic acid* ($C_5H_{11}\cdot TeO\cdot OH$) was obtained by aerial oxidation of di-*n*-amyl telluride and the ethyl and *l*-menthyl esters of *n*-amyltelluroacetic acid ($C_5H_{11}\cdot Te\cdot CH_2\cdot CO_2H$).

* Microanalyses by Dr. Strauss of Oxford.

The complex $3(C_5H_{11})_2TeO,C_5H_{11}\cdot TeO_2H$ was obtained by oxidation of the telluride with hydrogen peroxide; $C_5H_{11}\cdot TeO\cdot CH_2\cdot CO_2Et,2C_5H_{11}\cdot TeO\cdot OH$ was obtained by the action of hydrogen peroxide on ethyl *n*-amyltelluroacetate. The tellurinic acid and $C_5H_{11}\cdot TeO\cdot CH_2\cdot CO_2Et,2C_5H_{11}\cdot TeO\cdot OH$ decomposed without melting at 200° and were insoluble in water and in organic solvents. The substance $3(C_5H_{11})_2TeO,C_5H_{11}\cdot TeO_2H$ melted with decomposition at about 150° and was soluble only in alcohol and in chloroform. On the other hand, derivatives of quadrivalent tellurium were prepared which had true melting points and were soluble in a number of organic solvents. These observations are in good agreement with those made in the previous work.

Since it was previously suggested that the decomposition of the telluroxides involved the methylene group adjacent to the tellurium atom, the preparation of di-*tert.*-butyl telluride was attempted with the object of studying its oxidation products. The oil assumed to be the crude telluride rapidly decomposed, depositing tellurium. On treatment of the residual liquid with water, a brown solid separated. This contained a very high proportion of tellurium, and on heating suddenly evolved copious black fumes, leaving a residue of tellurium dioxide. Its properties, therefore, resembled those of ditelluromethane (Morgan and Drew, J., 1925, 127, 533), but were not further examined, as the compound was unsuitable for the present investigation.

Experimental.

Di-*n*-amyl telluride, b. p. 138—140°/18 mm., 98—100°/2 mm., was obtained in 55% yield from amyl bromide by the method used by Balfe, Chaplin, and Phillips (*loc. cit.*) (Found: Te, 46·7. Calc. for $C_{10}H_{22}Te$: Te, 47·3%). The telluride reacted with an equimolecular proportion of (*a*) methyl iodide, giving methyldi-*n*-amyltelluronium iodide, m. p. 70° after recrystallisation from ether–light petroleum; (*b*) ethyl bromoacetate, giving the *ethyl* ester of di-*n*-amyltelluretine bromide, m. p. 50° after recrystallisation from hot light petroleum (Found: Te, 28·9; Br, 17·7. $C_{14}H_{29}O_2BrTe$ requires Te, 29·2; Br, 18·3%); (*c*) ω-bromoacetophenone, giving phenacyldi-*n*-amyltelluronium bromide, m. p. 84° after recrystallisation from aqueous acetone. These three telluronium compounds were freely soluble in organic solvents except ether and light petroleum.

Ethyl n-*amyltelluroacetate*, b. p. 140—150°/17 mm. (Found: Te, 45·6. $C_9H_{18}O_2Te$ requires Te, 44·7%), obtained by thermal decomposition of the ethyl ester of di-*n*-amyltelluretine bromide, reacted with benzoyl peroxide (1 mol.) in chloroform solution to give the corresponding *dibenzoate*, $C_5H_{11}\cdot Te(OBz)_2\cdot CH_2\cdot CO_2Et$, m. p. 77—78° after recrystallisation from aqueous alcohol (Found: C, 52·1; H, 5·4. $C_{33}H_{18}O_6Te$ requires C, 52·3; H, 5·4%). Attempts to isolate hydrolysis products after treatment of the dibenzoate with alkali were unsuccessful.

A dibenzoate was obtained in a similar way from *l*-methyl *n*-butyltelluroacetate by Balfe, Chaplin, and Phillips (*loc. cit.*); other examples of dibenzoate formation by reaction with benzoyl peroxide are from *cyclo*hexene (Gelissen and Merimans, *Ber.*, 1926, **59**, 666) and from triphenylbismuthine and triphenylstibine (Challenger and Wilson, J., 1927, 209).

Heat was generated when di-*n*-amyl telluride and *l*-menthyl bromoacetate were mixed in equimolecular proportion, but the pasty product could not be crystallised. On thermal decomposition it yielded *n*-amyl bromide and the *l*-menthyl ester of *n*-amyltelluroacetic acid (b. p. 78—85°/17 mm.).

Di-*n*-amyl telluride in acetone solution with equimolecular proportions of (*a*) mercuric chloride gave a precipitate containing two components which could not be separated (the precipitate was partly liquefied at 80°, and the residual solid liquefied at 135°), (*b*) mercuric iodide gave, after removal of acetone, a viscous product which could not be crystallised and on thermal decomposition regenerated the reactants, (*c*) mercuric bromide deposited crystals of the addition *compound*, m. p. 88° after recrystallisation from acetone (Found: C, 18·6; H, 3·3. $C_{10}H_{12}Br_2HgTe$ requires C, 19·0; H, 3·4%).

Crystalline substances could not be obtained from the viscous products formed by addition of iodine in chloroform or carbon tetrachloride solution to di-*n*-amyl telluride or ethyl *n*-amyltelluroacetate.

n-*Amyltellurinic Acid.*—The white solid which separated on exposure of di-*n*-amyl telluride or the ethyl or *l*-menthyl ester of *n*-amyltelluroacetic acid to air was insoluble in water and all organic solvents, soluble in aqueous sodium hydroxide, and reprecipitated by a slight excess of acid. After being washed with light petroleum, it decomposed between 200° and 220° (Found:

C, 26·4; H, 5·3; Te, 55·4; equiv., 222. $C_5H_{12}O_2Te$ requires C, 25·9; H, 5·2; Te, 55·5%; equiv., 231).

On addition of perhydrol (10 c.c.) to di-*n*-amyl telluride (10 g.) a white *solid* separated, which was soluble in alcohol or chloroform and insoluble in other solvents. After recrystallisation from chloroform–acetone (yield, 3·3 g.) it had m. p. 144° (decomp.) (Found: C, 38·2; H, 7·3; Te, 45·1. $C_{35}H_{78}O_5Te_4$ requires C, 38·6; H, 7·1; Te, 46·8%). A similar product, with a somewhat higher m. p. (152°, decomp.), was obtained when the reaction was carried out in acetone solution (Found: C, 38·6; H, 7·1%).

The white *solid* (4·5 g.) which separated when perhydrol (20 c.c.) was added to ethyl *n*-amyltelluroacetate (5 g.) was washed with hot alcohol and dried. It was insoluble in all solvents and in alkali, but soluble in dilute acid; it decomposed at 200° (Found: C, 29·2; H, 5·4; Te, 50·2. $C_{19}H_{42}O_7Te_3$ requires C, 29·8; H, 5·1; Te, 50·9%).

*Attempted Preparation of Di-*tert.*-butyl Telluride.*—The method described by Balfe, Chaplin, and Phillips (*loc. cit.*) was employed, using 34 g. of sodium hydroxide, 44 g. of "rongalite," 500 c.c. of water, 20 g. of tellurium, and 46 g. of *tert.*-butyl chloride in 200 c.c. of ethyl alcohol. The oil obtained from the dried ethereal extract was stored under coal gas. It rapidly deposited tellurium. On addition of water to the residual liquid, a brown solid separated, which gradually became black (Found: C, 16·0; H, 3·3; Te, 80·0%).

Thanks are due to the Government Grants Committee of the Royal Society and Imperial Chemical Industries, Ltd., for grants, to the High Commissioner for India for maintenance grants (K. N. N.), and to Dr. J. Kenyon, F.R.S., for his interest in this work.

BATTERSEA POLYTECHNIC, LONDON, S.W.11. [*Received, October 30th*, 1940.]

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17. *Qualitative Semimicro-analysis with Reference to Noyes and Bray's System: The Thallium Group.*

By CHRISTINA C. MILLER.

A scheme of analysis differing from that of Noyes and Bray has been evolved for the detection and estimation of 0·25—50 mg. of silver and lead, 0·25—10 mg. of thallium, and some bismuth in mixtures containing a maximum of 50 mg. of the combined metals. The main features are the dissolution of the metallic bromides in hydrobromic acid, the detection of thallium with rhodamine-B in the presence of lead and bismuth and some silver, the extraction of thallium (III) bromide by means of *n*-butyl acetate, the detection of silver in a cyanide solution with *p*-dimethylaminobenzylidenerhodanine, the simultaneous detection of bismuth and lead with thiourea, and the final confirmation of lead as lead rhodizonate.

IN two recent papers (Miller and Lowe, J., 1940, 1258, 1263) schemes of semimicro-analysis were submitted for three groups of Noyes and Bray's system ("A System of Qualitative Analysis for the Rare Elements," 1927). The present paper describes an extension of the methods to the thallium group, which has already been analysed on the micro-scale by Benedetti-Pichler and Spikes (*Mikrochem.*, 1936, **19**, 239).

The essential components of the thallium group are thallium (I), lead, and silver, with perhaps some bismuth, which are precipitated as their bromides when hydrobromic acid is added to the filtrate from the precipitate composing the tantalum, the tungsten, and the gold group. Although it was anticipated from a consideration of Noyes and Bray's work (*op. cit.*, pp. 44, 48, 123, 371) that only a fraction of the silver in a mixture would be present at this stage, that 1—2 mg. of lead would remain in the solution, and that bismuth precipitated in excess of 25 mg. might be completely removed in the subsequent washing process (see, however, p. 74), yet provision was made for the detection and estimation of 0·25—50 mg. of lead and silver, 0·25—10 mg. of thallium, and a moderate amount of bismuth.

EXPERIMENTAL.

Preparation of the Group for Analysis.—In order to precipitate the bromides in solutions comparable with those of Noyes and Bray, mixtures of the nitrates of lead, silver, and bismuth

were evaporated to fumes with 0·35 ml. of 9N-perchloric acid. Thallium (I) perchlorate, 0·5 ml. of 24N-formic acid, and water were then added to make a volume of 1·2 ml. The bromides were precipitated and washed with dilute, bromine-free hydrobromic acid, one-tenth of Noyes and Bray's quantities being used, and analysed according to the tabulated scheme. As a check on the recovery of bismuth and lead, the centrifugates containing bismuth and unprecipitated lead were treated with nitric acid and evaporated to dryness, dissolved in 2N-nitric acid, and examined for the metals as described in the group analysis.

Thallium Group.

(The figures in parentheses are referred to in " Notes on Methods and Tests.")

Precipitate. Pb, Tl^{I}, Ag, and Bi (probably) bromides. Boil with 0·5 ml. of 9N-HBr and a small excess of Br_2 to form Tl^{III}. Gradually dilute with 1 ml. of water and remove precipitated AgBr by centrifuging (1). To 0·05 ml. of the solution add 0·05 ml. each of 9N-HBr, H_2O, and then 2% aq. Na_2HAsO_3. Finally, add dropwise a small excess of rhodamine-B (1% in 3N-HBr), and centrifuge. A red precipitate shows **Tl** (2). Assess. If Tl is present, remove $TlBr_3$ from the remainder of the solution by extracting thrice with 0·5 ml. of *n*-butyl acetate (3). Evaporate the aq. layer to ~0·5 ml., cautiously add concentrated HNO_3 in excess, expel Br_2, and take just to dryness. Extract once with 0·5 ml. of hot 2N-HNO_3, and twice with 0·25 ml. of the cold acid (4). Wash the precipitate of AgBr with a little water and reject the washing.

Precipitate. AgBr. Estimate roughly. Dissolve in 0·2—1·5 ml. of 5% aq. KCN, according to the bulk of the precipitate (1 ml. dissolves ~40 mg. of Ag), and centrifuge. Mix 0·05 ml. with 0·5 ml. of *p*-dimethylaminobenzylidenerhodanine (saturated in CH_3·OH), add 2 drops of 2N-HNO_3, and centrifuge. A reddish-purple precipitate shows **Ag**. If an excess of reagent is not indicated (yellow centrifugate), repeat the test with 2·5 ml. of the reagent. Assess (5).

Any residue in the KCN extract may be dissolved in 2N-HNO_3 and examined for Pb and Bi.

Note.—If desired, part of the group precipitate may be at once treated with HNO_3 to remove Pb, Bi, and Tl, and tested for Ag as above.

Solution. Contains $Pb(NO_3)_2$ and $Bi(NO_3)_3$ in 1 ml. Test portions as follows.

(*a*) To 0·5 ml. of the *cold* solution add ≮0·5 ml. of thiourea (saturated in N-HNO_3 at 20°), stir, and centrifuge. A precipitate, white in the absence of Bi, yellow in its presence, shows **Pb**, and a yellow solution, **Bi**. Estimate Pb (6). To confirm a small amount of Pb (<1 mg.) wash the precipitate once with the reagent, and twice with ethyl alcohol to remove free acid. Dissolve in 1—2 drops of hot water, add excess of a fresh, saturated aq. solution of sodium rhodizonate, and centrifuge. A reddish-purple precipitate shows **Pb**. Estimate. Finally, add to the separated precipitate, without stirring, a drop of 2N-HCl, which changes its colour to blue-purple and partly dissolves it (7).

(*b*) If the presence of Bi has been shown in (*a*), dilute 0·1—0·5 ml. to 2 ml. with 1—2N-HNO_3, and add an excess of solid thiourea. If necessary, warm to keep Pb in solution, and compare with standards for **Bi** (8).

Notes on Methods and Tests.

Note 1. 0·5 Ml. of 9N-hydrobromic acid, which dissolved large amounts of lead and thallium (III) bromides, and ~10 mg. of silver as silver bromide, was ample for the extraction of all the thallium, but more could be used, if desired. Dilution to 3N reprecipitated most of the silver, and gave appropriate conditions for the rhodamine-B test and the removal of thallium bromide.

Note 2. Eegriwe (*Z. anal. Chem.*, 1927, **70**, 400) found a 0·01% aqueous solution of rhodamine-B to be a sensitive reagent for thallium (III) and certain other metals. Miller and Lowe (*loc. cit.*) enhanced the selectivity of the reagent by employing it in fairly concentrated hydrochloric acid solutions. For the detection and estimation of thallium (III), in the presence of large amounts of lead, excellent results were obtained by substituting 3N-hydrobromic acid, in which lead bromide was somewhat soluble. As little as 2γ of thallium was detectable in 1 ml. of 3N-hydrobromic acid containing 10 mg. of lead or bismuth, and silver bromide to saturate the solution. One drop of the 1% reagent solution precipitated 25γ of thallium. Bromine, which formed a red precipitate with the reagent, was instantaneously destroyed by sodium arsenite, which did not reduce thallium (III) in the strongly acid solution.

Note 3. This method of extraction was extremely simple, and the removal of thallium (≮10 mg.) virtually complete. Lead bromide was insoluble and bismuth bromide only slightly soluble.

Note 4. The evaporation was rapidly effected in the centrifuge tube, placed in a boiling water-bath, if a current of air played on the surface. The nitric acid treatment separated

even minimal amounts of lead and bismuth nitrates very satisfactorily from 50 mg. of silver, and small amounts of silver bromide were retained as such. Although large quantities of lead and bismuth might leave large precipitates of silver bromide slightly contaminated, the subsequent test for silver was unaffected.

Note 5. The test for silver with *p*-dimethylaminobenzylidenerhodanine was based on that described by Feigl (" Qualitative Analyse mit Hilfe von Tüpfelreaktionen," 1938, 159), but provided for an estimation. The reagent was prepared in methyl alcohol because it gave a clear solution with a cyanide solution of silver bromide, and was more sensitive than the acetonic reagent. For the estimation of silver it was essential to add an excess of the reagent *before* the nitric acid, and to compare with standards prepared from silver bromide, *not* silver nitrate, dissolved in aqueous potassium cyanide. Although the test was at least five times less sensitive with the bromide, it was adequate for the present purpose, and simple to apply. As somewhat erratic results were occasionally obtained in testing for silver bromide in very small amounts, it was inadvisable to have $< 25\gamma$ of silver per drop of the cyanide solution. 0·5 Ml. of the reagent served for 200γ of silver. The large proportion of methyl alcohol in the final solution prevented deposition of the reagent itself.

Note 6. Mahr and Ohle's method of separating lead from a large number of metals by precipitating its bulky complex with thiourea, in a solution 1—2N in nitric acid, was very successful (*Z. anorg. Chem.*, 1937, **234**, 224). Thallium reacted similarly and more readily and had to be absent. The presence of silver was unlikely, but its complex is soluble in an excess of the reagent. 5 Mg. of bismuth gave only a yellow solution, but coloured the lead precipitates yellow, and slightly retarded their formation. It did not seriously affect their bulk, and 50γ of lead were detectable. It was advisable to confirm the presence of lead in a small precipitate (see Note 7).

Note 7. The thiourea complex of lead was not obviously soluble in ethyl alcohol, but dissolved readily in a small volume of water, giving an approximately neutral solution. As a distinctive confirmatory test for lead its complexes with sodium rhodizonate were formed. Very weakly acid solutions of lead salts give reddish-purple precipitates with sodium rhodizonate (cf. Kolthoff, *Pharm. Weekblad*, 1925, **62**, 1017, through *Chem. Zentr.*, 1926, I, **97**, 448). Just as treatment with 2N-hydrochloric acid caused the brownish-red rhodizonate complex of barium to change to carmine (cf. Miller, J., 1940, 401), so the reddish-purple complex of lead was changed to a characteristic blue-purple one, which slowly dissolved. No other metal examined behaved in this manner. The dissolved thiourea complex of lead was readily transformed into the reddish-purple rhodizonate complex, on the bulk of which lead could be assessed, and thence to the highly distinctive blue-purple complex as a final check. Although the presence of thallium and silver in the lead–thiourea complex was unlikely, the behaviour of their corresponding complexes was examined. The thallium complex remained acid and decolorised sodium rhodizonate, and the silver complex gave a dirty-brown, non-settling precipitate. Bismuth contaminating the lead–thiourea complex exerted no influence. It was unnecessary to have more than 500γ of lead for the test (one drop of the reagent solution sufficed for 40—50γ), and 50γ could be carried through the whole process. Attempts to detect and estimate lead directly with sodium rhodizonate, in the presence of thallium and bismuth, were not successful.

Note 8. Amounts of bismuth ranging from 5γ to 2·5 mg. could be satisfactorily detected and estimated in 2 ml. of 1—2N-nitric acid, provided that an excess of thiourea was added, and that a short time was allowed for full colour development (cf. Dubský, Okáč, and Trtílek, *Mikrochem.*, 1935, **17**, 332). Suitable portions of solutions containing large amounts of bismuth were examined. The dissolved complexes of lead (and thallium) were without influence.

Analysis of Mixtures.—In order to test the analytical scheme a number of mixtures were prepared and selected at random. The results are given in the table, the figures referring to the weights in mg.

It will be noted that a maximum of 1 mg. of lead was found in the solution from the group precipitation. An amount of lead well below this figure was, however, actually found in the group, presumably because it was carried down by a large group precipitate (No. 7). The removal of bismuth, by washing the group precipitate with cold N-hydrobromic acid, might be by no means complete (No. 3), and bismuth must be allowed for in the group analysis. Noyes and Bray's experiments on the solvent effect of hydrobromic acid on bismuth bromide (cf. p. 72) were made in the absence of the other metallic bromides.

The estimations of all the metals were considered satisfactory, and no metal absent from the mixtures was erroneously reported.

	Element.	Tl.	Ag.	Pb. In group precipitate.	Pb. In solution from group.	Bi. In group precipitate.	Bi. In solution from group.
1	Present	7	—	20		20	
	Found	7·5	0	20	0·5	1	20
2	Present	10	3	—		—	
	Found	10	2	0	0	0	0
3	Present	0·5	5	0·5		40	
	Found	0·5	10	0·1	0·05	10 †	25
4	Present	0·25	20	2		20	
	Found	0·25	20	0·5	1	2 ‡	22
5	Present	—	15	25		10	
	Found	0	12	22 *	0·5	0·15	10
6	Present	2	0·25	35		10	
	Found	2·5	0·3	34	0·5	0·5	10
7	Present	10	40	0·25		—	
	Found	10	40	0·5	Trace	0	0
8	Present	0·25	50	—		—	
	Found	0·25	50	0	0	0	0

* 1·5 mg. in AgBr. † 50γ in AgBr. ‡ 25γ in AgBr.

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THE UNIVERSITY, EDINBURGH, 9. [*Received, December 4th*, 1940.]

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18. *Amino-sulphonic Acid Analogues of Natural Amino-carboxylic Acids.*

By HENRY MCILWAIN.

Many substances which inhibit the growth of micro-organisms appear to do so by interfering with substances essential in reactions involved in growth. In some cases there is evidence that this occurs because similarity in structure between the essential substance and the inhibitor causes the latter to block enzymes whose normal substrate is the essential metabolite in question. Sulphanilamide interferes with *p*-aminobenzoic acid in this manner, and pyridine-3-sulphonic acid and its amide with nicotinic acid and its derivatives (Woods, *Brit. J. Exp. Path.*, 1940, **21**, 74; McIlwain, *ibid.*, p. 136). With the intention of making further inhibitory compounds, the amino-sulphonic acids described below have been prepared; they are related in the above manner to α-amino-acids and to β-alanine, which are known to be essential to many pathogenic micro-organisms.

IT can now be accepted that the products of the action of aqueous ammonia on aldehyde bisulphite compounds are α-amino-sulphonic acids (Raschig and Prahl, *Annalen*, 1926, **448**, 265; Backer and Mulder, *Rec. Trav. chim.*, 1933, **52**, 454). The objections raised by Schroeter (*Ber.*, 1933, **66**, 1038) have been answered by Backer and Mulder (*Rec. Trav. chim.*, 1934, **53**, 1120) and by Rumpf (*Compt. rend.*, 1937, **204**, 592). The amino-sulphonic acid analogues of many of the naturally occurring α-amino-carboxylic acids are thus easily accessible, and α-amino-methane-, -ethane-, -*iso*butane-, *iso*pentane-, -phenyl-methane-sulphonic acids, and an amino-sulphonic acid derivative of citronellal, have been prepared as bacterial inhibitors for the reason outlined above. The first four members correspond to glycine, alanine, valine, and leucine, several of which are known to be limiting factors in the growth of some pathogenic organisms.

α-Amino-sulphonic acids are reported as unstable in aqueous solution, but experiments with typical members have shown that no appreciable decomposition occurred under the conditions of biological testing (p_H 7·6 at 37°) with the exception of the citronellal derivative, though extensive decomposition occurred at 100°.

Of the aliphatic amino-acids other than α-amino-acids, β-alanine is that known to be

of greatest importance in bacterial nutrition. The corresponding amino-sulphonic acid, taurine, is already well known, and it was decided to prepare also the corresponding *sulphonamide*. This was unsuccessfully attempted by the action of ammonia on β-chloroethanesulphonyl chloride, but conveniently achieved through the *carbobenzyloxy*-derivative, a method not previously used in connection with amino-sulphonic acids. The sulphonamide was stable to the reducing conditions necessary for removal of the carbobenzyloxy-group.

Results of bacteriological work with the amino-sulphonic acids have in some cases shown specific inhibitory relations with amino-carboxylic acids, and will be reported in full elsewhere.

Experimental.

Aminomethanesulphonic acid was prepared according to Raschig and Prahl (*loc. cit.*) in 25% yield and recrystallised from hot water; m. p. 210° (decomp.) (Found: N, 12·6; S, 28·9; alkali equiv., 111·5. Calc. for CH_5O_3NS: N, 12·6; S, 28·8%; equiv., 111).

α-Aminoethanesulphonic acid was prepared according to Backer and Mulder (*loc. cit.*, 1934) in 33% yield and recrystallised from water as detailed for the butane compound [Found: N (Kjeldahl), 11·05; N (nitrite), 11·1; S, 25·6. Calc. for $C_2H_7O_3NS$: N, 11·2; S, 25·6%].

α-*Amino*iso*butanesulphonic Acid.*—The corresponding hydroxy-compound (10 g.; prepared from freshly distilled *iso*butaldehyde and 5N-sodium bisulphite) was shaken at room temperature with aqueous ammonia (20 ml., *d* 0·88) for 1 hour, the mixture cooled, and cold 10N-sulphuric acid added so that the temperature remained below 20°, and until the p_H reached 3·5—4. The *amino-sulphonic acid* (4·5—5·5 g.), which separated in colourless crystals, was filtered off after ½ hour (on longer standing it decomposed), washed with 50% alcohol, alcohol, and ether, and recrystallised by dissolving it in water (15 ml.) at 70° by vigorous shaking (at higher temperatures it decomposed; solution should be effected in 5 minutes) and allowing the filtered solution to stand in a vacuum over calcium chloride (Found: N, 9·2; S, 20·6. $C_4H_{11}O_3NS$ requires N, 9·2; S, 20·9%).

α-*Amino*iso*pentanesulphonic acid*, prepared from the hydroxy-compound (10 g.) and isolated as described for the *iso*butane compound, was obtained as a finely crystalline sludge (4·5—6 g.). Recrystallised from water (20 ml.) at 80°, it formed plates resembling leucine (Found: N, 8·3; S, 19·2. $C_5H_{13}O_3NS$ requires N, 8·3; S, 19·2%).

α-*Aminophenylmethanesulphonic Acid.*—Ammonium sulphite (15 g.) was dissolved in water (15 ml.) by warming and shaken with freshly distilled benzaldehyde (10·5 ml.) at 40—50°; after ½ hour the solution was cooled in ice, and cold 10N-sulphuric acid added gradually until the p_H was 3. The granular *amino-acid* (4 g.) was filtered off after 2 hours, washed with 50% alcohol, and recrystallised from water (20 ml.) as above, forming colourless prisms, m. p., with loss of water, 123° (Found: N, 6·8; S, 15·5. $C_7H_9O_3NS,H_2O$ requires N, 6·8; S, 15·6%). The dried material melted at 185° (Found: N, 7·5. $C_7H_9O_3NS$ requires N, 7·5%).

Amino-sulphonic Acid from Citronellal.—The hydroxy-compound (10 g., prepared from redistilled citronellal and 5N-sodium bisulphite) was treated with aqueous ammonia, and the product (4—5 g.) separated, as described above. The *acid* crystallised from water in soft colourless plates, m. p. 142—143° (Found: N, 5·95; S, 13·9. $C_{10}H_{21}O_3NS$ requires N, 6·0; S, 13·6%).

Stability of Amino-sulphonic Acid Solutions.—This was determined by titration of the sulphur dioxide liberated from M/50-solutions of the amino-sulphonic acids in air-free buffer of p_H 7·6, heated under various conditions in oxygen-free nitrogen. No decomposition was found with aminoethane- and aminobutane-sulphonic acids at 37° or 50° in 1—4 days; aminopentanesulphonic acid decomposed to the extent of 2% after 3 days at 37° and 5% after 2 days at 50°. The citronellal derivative decomposed at room temperature in 1 day.

Sodium N-*Carbobenzyloxytaurine.*—Taurine (8 g.) was dissolved by warming in water (40 ml.), the solution stirred with ice cooling, and sodium bicarbonate (11·2 g.) added, followed by benzyl chloroformate [from benzyl alcohol (12 ml.) and carbonyl chloride (Bergmann and Zervas, *Ber.*, 1932, **65**, 1192)] during 10 minutes. Stirring was continued at room temperature for 4 hours, the solution extracted three times with its own bulk of ether, and the aqueous layer made acid with hydrochloric acid and evaporated under reduced pressure to about 60 ml.; it then began to crystallise. The solution was warmed and filtered from sodium chloride; the *product* (16 g.) separated on cooling. A little was recrystallised from aqueous alcohol (Found: N, 4·85. $C_{10}H_{12}O_5NSNa$ requires N, 4·8%).

N-*Carbobenzyloxytaurine Amide*.—The sodium salt (8 g.) and phosphorus pentachloride (8 g.), both finely ground, and benzene (80 ml.) were refluxed for 25 minutes, and the benzene and phosphorus oxychloride removed under reduced pressure. The sulphonyl chloride was extracted from sodium chloride with dry benzene (250 ml.), this solution cooled in ice, and an excess of dry ammonia passed in; it was then refluxed in a slow stream of the gas for 2 hours. The product was exhaustively extracted with hot benzene, from which the *amide* (4 g.) separated on concentrating and cooling. It was recrystallised from benzene or aqueous methanol, forming colourless prisms, m. p. 133° (Found: N, 10·6. $C_{10}H_{14}O_4N_2S$ requires N, 10·8%).

Taurine Amide Hydrochloride.—Finely ground carbobenzyloxytaurine amide (2 g.) and palladium-black (0·1 g.; Willstätter, *Ber.*, 1921, **54**, 123) were shaken with water (20 ml.), methanol (20 ml.), and glacial acetic acid (6 ml.) in a stream of hydrogen. Evolution of carbon dioxide and solution of the solid were complete in ½ hour; the palladium was then filtered off, and the solvents removed under reduced pressure and by standing in a vacuum over sodium hydroxide. The residue was dissolved in alcohol (10 ml.), and saturated alcoholic hydrogen chloride added gradually with scratching till no further material separated. The *hydrochloride* was collected; it crystallised from hot alcohol in colourless plates (1·2 g.), m. p. 133° (Found: C, 15·25; H, 5·6; S, 19·7. $C_2H_9O_2N_2ClS$ requires C, 15·0; H, 5·6; S, 19·9%).

This compound has been prepared by Miller, Sprague, Kissinger, and McBurney (*J. Amer. Chem. Soc.*, 1940, **62**, 2099) by a different method.

This work was carried out in the Department of Bacterial Chemistry (Medical Research Council), in the Bland Sutton Institute of Pathology and the Courtauld Institute of Biochemistry, during the tenure of a Leverhulme Research Fellowship. My thanks are due to Mr. D. E. Hughes for carrying out most of the analyses reported.

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19. *Modified Cinchona Alkaloids. Part VIII. Niquine.*

By WILLIAM SOLOMON.

Niquine, niquidine, and "δ-cinchonine," transformation products of quinine, quinidine, and cinchonine respectively, form a distinct class of analogously constituted, modified cinchona alkaloids. The first two are now shown to be stereoisomerides, and a study of the oxidation products of *dihydroniquine*, parallel with one which was carried out with dihydroniquidine (Part VII), confirms the structure, which, already assigned to the latter, must be common to both substances.

THE action of mineral acids on the four typical cinchona alkaloids, (I), produces substances which are for the most part either structural isomerides or hydration products of the parent bases or of their demethylation products (Part IV, J., 1937, 592). Similar results are obtained in dehalogenating the halogenodihydro-compounds obtained by the addition of hydrogen halide to the vinyl group. In this case, however, the products include a different type of substance (II), in the formation of which the quinuclidine ring is ruptured with the production of a secondary amino-group; examples of this kind are the conversion of quinine into niquine (Skraup, *Ber.*, 1892, **25**, 2909; *Monatsh.*, 1893, **14**, 428), of cinchonine into δ-cinchonine (Jungfleisch and Léger, *Compt. rend.*, 1894, **118**, 30), afterwards recognised as an analogue of niquine (Langer, *Monatsh.*, 1901, **22**, 157), and of quinidine into niquidine (Domanski and Suszko, *Bull. Acad. Polonaise*, 1935, *A*, 457). It is not certain that any modification of the fourth alkaloid, cinchonidine, belongs to this class. These substances are formed in pairs of geometrical isomers; *e.g.*, "δ-cinchonine" is the α-cinchonhydrine of Léger (*Compt. rend.*, 1919, **169**, 797), and is accompanied by a β-isomer; "niquidine" is a mixture of niquidine and *iso*niquidine (Part VI, J., 1939, 240); and Skraup claimed an "*iso*niquine," but the present author has been unable to isolate this substance.

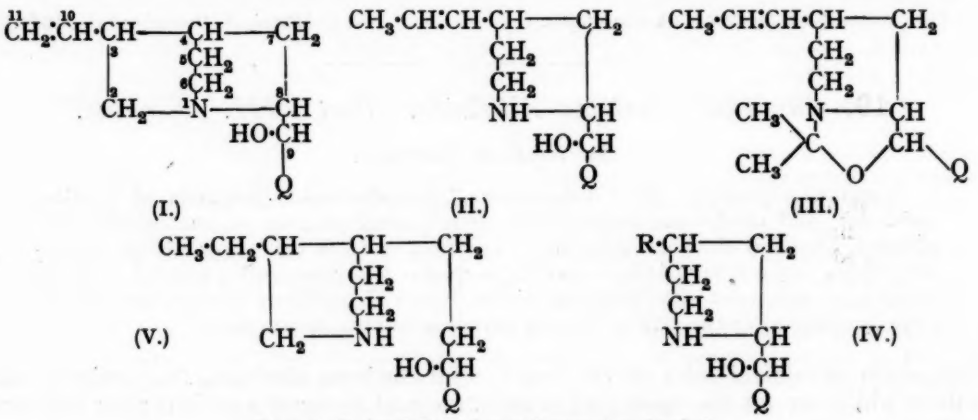
The recognition that these bases are analogous amongst themselves implies their stereochemical correspondence, and it seems probable that niquidine is 6-methoxy-α-cinchonhydrine and *iso*niquidine has the configuration of the β-isomer. That niquine

and one of the niquidines must be stereoisomers is now verified by the interconversion of their dihydro-derivatives (p. 82).

Until the results of the work on niquidine were obtained (Part VI, *loc. cit.*; Part VII, J., 1939, 1294), the constitution of these bases remained unsettled. Skraup observed that a reducing substance, now known to be formaldehyde, was produced in the reaction which gave rise to niquine, and proposed for the latter the formula $C_{19}H_{24}O_2N_2$, which contains one carbon atom less than quinine and is now known to be correct.

The information accumulated prior to 1939 may be summarised as follows: (*a*) niquine and its analogues retain intact the (methoxy)quinoline nucleus and central hydroxyl group of their parent alkaloids, and (*b*) the quinuclidine nitrogen atom becomes secondary, indicating rupture at one of three points. Confirmation of the splitting of a carbon atom as formaldehyde (Part VI) and the isolation of β-propylglutaric acid from the products of oxidation of dihydroniquidine with hydrogen peroxide (Part VII) sufficed to formulate niquidine as (II). The position of the forgotten double bond (see Léger, *loc. cit.*; *Ann. Chim.*, 1920, **14**, 59, 129) was confirmed in the case of niquidine (Part VI) and is now once more verified with niquine, by showing the presence of one *C*-methyl group (Kuhn–Roth). The existence of geometrical isomerides, which could be hydrogenated to one and the same dihydro-derivative, also supported the view that the double bond had shifted from the terminal carbon atom.

For the work now described, quinine was transformed into niquine in *ca.* 33% yields, concentrated hydriodic acid being used as the hydrohalogenating agent, and aqueous alcoholic potassium hydroxide for the dehalogenation. A further 33% of the quinine



(I.) (II.) (III.) (V.) (IV.)

Q = 4-Quinolyl or 6-methoxy-4-quinolyl.

was isolated as β-*iso*quinine; the remainder was uncrystallisable. In spite of the findings of several authors single attempts to de-iodinate with silver nitrate or with ammonia gave lower yields of niquine. This modified quinine alkaloid is now fully characterised. On catalytic hydrogenation it takes up two atoms of hydrogen, furnishing *dihydroniquine* (IV; R = propyl), which on boiling in dilute acetic acid is stereochemically converted into a mixture from which dihydroniquidine and *epi*-C_9-dihydroniquidine (Part VI) have been isolated, and which does not give the toxin reaction of Bachstez and Caro (*Arch. exp. Path. Pharm.*, 1932, **164**, 316); it seems that the modified cinchona alkaloids of this class are incapable of undergoing the Pasteur reaction to toxins (compare Part VI, and Suszko, *Bull. Acad. Polonaise*, 1925, *A*, 129, but contrast Domanski and Suszko, *loc. cit.*), but epimerise on boiling with dilute acetic acid. In view of the present results, moreover, this epimerisation seems to involve both carbon atoms 8 and 9, and a fourth epimeride, *epi*-C_9-dihydroniquine, probably remains undiscovered in the crude products obtained both from dihydroniquine and from dihydroniquidine.

Dihydroniquine, like dihydroniquidine, has now furnished quininic acid and β-propylglutaric acid on oxidation with hydrogen peroxide.

When niquine is heated with acetone, iso*propylideneniquine* (III) is formed. This substance does not react with methylmagnesium iodide in hot or cold anisole solution (Zerewitinoff), and thus differs from niquine, which furnishes one molecule of methane from the hydroxyl group in the cold and a further molecule from the imino-group at 130°. These results not only afford further evidence of the presence of both hydroxyl and the imino-group in niquine, but also show that (III) must be the formula of *iso*propylideneniquine. This compound, which is analogous to the acetone derivatives in the sugar series rather than to those formed by certain *iso*quinoline alkaloids, such as berberine-acetone and anhydrocotarnineacetone, is very unstable in acid solution, being readily hydrolysed to niquine and acetone, and attempts to prepare its salts furnish only the corresponding niquine salts and free acetone. It appears to be unusual for acetone to condense in this way with compounds having, not two adjacent hydroxyl groups, but one hydroxyl and one amino-group. Attempts to prepare the corresponding methylene derivative by treating niquine with formaldehyde gave inconclusive results.

Although the constitutions of niquine and its analogues have now been elucidated, the nature of the remarkable reaction which gives rise to these modified cinchona alkaloids remains obscure.

In bird malaria niquine and niquidine show a degree of activity almost equal to that of quinine (*Biochem. J.*, 1938, **32**, 47). This result is in good agreement with the theory of King and his co-workers (*Proc. Roy. Soc.*, 1938, *B*, **125**, 49, 60; J., 1940, 1307, 1315), according to which antiplasmodial activity is exhibited by 6-methoxyquinoline carbinol-amines of the type (IV; R = H) or, more generally, of the type Q·CH(OH)·CH(NR′R″)·, to which the natural cinchona alkaloids belong. Inactivity results if the basic centre is removed to a remote position in the side chain, as in the dihydroquinicinols (V), which are of the type Q·CH(OH)·$[CH_2]_4$·CH(NR′R″)·. Niquine (IV; R = propenyl) and dihydroniquine (IV; R = propyl) clearly belong to the first of these two categories.

Experimental.

The m. p.'s are corrected. The optical rotations refer to M/40-solutions and were carried out with or are calculated for the anhydrous material.

Iododihydroquinine Dihydriodide (compare Skraup, *loc. cit.*; Schubert and Skraup, *Monatsh.*, 1891, **12**, 669).—Anhydrous quinine (20 g.) was heated with hydriodic acid (120 c.c., *d* 1·65—1·7, decolorised by heating with red phosphorus) for 1·5 hours on a water-bath. The yellow crystalline product was cooled, filtered off, and washed with alcohol (yield, 35 g.). The salt began to decompose at about 220° and frothed at 238°.

De-iodination of Iododihydroquinine (Skraup, *loc. cit.*).—A solution of the foregoing dihydriodide (35 g.) in hot aqueous alcohol was treated with a hot aqueous solution of potassium hydroxide (54 g.) (total alcohol, 300 c.c.; total water, 250 c.c.) and refluxed for 1 hour. No formaldehyde was detected (dimedon bubbler) even after concentration of the solution to low bulk under diminished pressure. The product, consisting essentially of β-*iso*quinine and niquine, separated as a pale yellow oil, which, with progressive removal of alcohol, thickened to a plastic mass, becoming brittle on cooling. The separated mass was dissolved in hot alcohol (40 c.c.), and a warm solution of crystallised oxalic acid (14 g.) in acetone (50 c.c.) added. The crystalline niquine acid oxalate was filtered off and washed with alcohol; it contained potassium oxalate and the average yield was 10—15 g., corresponding to 6·5—9·5 g. of dry base. The salt was dissolved in dilute mineral acid and introduced in a slow thin stream into a well-stirred solution of caustic alkali. The resulting precipitate was crystalline, and was reconverted into the acid oxalate in aqueous alcoholic solution. Final purification was effected either by repeating this process a third time or by crystallising the base from ether or acetone. The original crude oxalate filtrate, when steam-distilled, furnished formaldehyde (isolated as the dimedon compound, m. p. and mixed m. p. 190—192°), and after treatment with sodium hydroxide yielded to ether a base, which crystallised (later fractions from acetone) and consisted of crude β-*iso*quinine, m. p. *ca.* 175° (total crystalline yield, about 7 g.) (see Part II, J., 1935, 968).

Niquine.—A solution of the base in ether, treated with a few drops of water, deposits a dense mass of feathery needles, m. p. *ca.* 100° (Found: loss in a vacuum over sulphuric acid, 9·0. Calc. for $C_{19}H_{24}O_2N_2,2H_2O$: H_2O, 10·3%); on prolonged heating it sinters at lower temperatures. The base crystallises from acetone in colourless needles, anhydrous when the

solvent is dry, but usually containing up to $1H_2O$. When solutions of niquine in acetone are kept or subjected to prolonged heating, some *iso*propylideneniquine (III) is formed (see below). Anhydrous niquine has m. p. 137° after sintering at 130°; it is very readily soluble in alcohol, readily in warm acetone, fairly readily in warm, dry ether, but sparingly in cold acetone and very sparingly in cold or moist ether or in water. Its solutions are colourless and show a blue fluorescence in dilute sulphuric acid. The solid base, which shows no tendency to turn yellow on exposure, dissolves in semicarbazide acetate solution without the production of an insoluble derivative, and crystallises unchanged from liquid phenylhydrazine. The base has $[\alpha]_D^{15°}$ — 248·0° (0·1N-sulphuric acid), or — 132·2° (alcohol) [Found for the anhydrous base: C, 73·3; H, 7·7; N, 9·0; OMe, 10·0; CMe (Kuhn–Roth), 8·4; OH (Zerewitinoff in anisole), 5·4; NH (temperature raised to 130° after preceding determination), 4·5. Calc. for $C_{19}H_{24}O_2N_2$: C, 73·0; H, 7·75; N, 9·0; OMe, 9·9; CMe, 8·65; OH, 5·4; NH, 4·8%]. Niquine hydrochloride crystallises from water or alcohol in yellowish needles, m. p. 197° (sinters), $[\alpha]_D^{15°}$ — 147·9° (water), or — 216·1° (0·1N-hydrochloric acid). The last figure corresponds to — 242° when recalculated for base. The air-dried salt contains a little less than $1H_2O$. The neutral sulphate crystallises from water, alcohol, or aqueous alcohol; it is sparingly soluble in cold water, more readily in alcohol or hot water, and crystallises best from water in thin platelets or flakes, which melt in their own water of crystallisation at about 65°, re-solidify, and then melt again at 160—170°. This salt separates from alcohol or aqueous alcohol in fluffy masses of needles, m. p. 160—170°. The acid sulphate crystallises from water in colourless needles, which sinter at 75° and melt at 165—168° (Found: loss at 65—70° in a vacuum, 23·0. Calc. for $C_{19}H_{24}O_2N_2,H_2SO_4,7H_2O$: H_2O, 23·5%). The anhydrous salt on exposure reabsorbs $2H_2O$. Skraup states that this salt contains 3·5 H_2O. It has $[\alpha]_D^{15°}$ — 187·5° (water), and this corresponds to — 246·4° for the base. *Niquine dihydrobromide* crystallises from water or alcohol in almost colourless, anhydrous needles, readily soluble in cold water, very readily in hot water, and sparingly in alcohol. It decomposes at 242—244° after darkening from about 190° onwards, and has $[\alpha]_D^{15°}$ — 161·7°, — 164·1° (water), equivalent to — 245·5° and — 249·2° expressed as base (Found: C, 48·2; H, 5·6; N, 5·9; Br, 33·5. $C_{19}H_{24}O_2N_2,2HBr$ requires C, 48·1; H, 5·5; N, 5·9; Br, 33·7%). Niquine acid oxalate crystallises from hot alcohol in colourless felted needles, m. p. 198—200° (decomp.) with previous darkening. It is very sparingly soluble in water, alcohol, and acetone (Found: C, 56·4; H, 5·8; N, 5·9. Calc. for $C_{19}H_{24}O_2N_2,2C_2H_2O_4$: C, 56·1; H, 5·7; N, 5·7%). The *acid dianisoyl-*d*-tartrate* separates from acetone in soft needles which sinter and decompose between 100° and 150°, $[\alpha]_D^{15°}$ — 153·0° (alcohol) (Found for air-dried salt: loss at 95° in a vacuum, 4·1. Found for salt so dried: C, 64·1; H, 6·05; OMe, 13·5. $C_{19}H_{24}O_2N_2,C_{20}H_{18}O_{10},2H_2O$ requires H_2O, 4·7%. $C_{19}H_{24}O_2N_2,C_{20}H_{18}O_{10}$ requires C, 64·1; H, 5·8; OMe, 12·7%). Niquine nitrate crystallises from 20% alcohol in colourless, tough, square plates of a stratified structure, m. p. 134—139°. It is soluble in alcohol but very sparingly in water.

iso*Propylideneniquine* (III) was prepared by heating niquine (1 g.) with acetone (10 c.c.) in a sealed tube at 105° for 7 hours and crystallising the product from acetone. It was also found in the mother-liquors from crystallisations of niquine from acetone, particularly when these had stood for some time. It separates from acetone in stout, transparent, faintly coloured, prismatic rods, unsymmetrically pointed at their ends, and of unsymmetrical heptagonal cross-section; when allowed to crystallise slowly, these may exceed 1 cm. in length. The substance, which tends to develop a faint pink tinge in solution or when ground, has m. p. 158—160°, $[\alpha]_D^{16°}$ — 123·3° (alcohol) or — 216° (0·1N-sulphuric acid), and undergoes no loss when heated at 115° in a vacuum [Found: C, 74·9; H, 7·8; N, 7·9; OMe, 8·9; CMe (Kuhn–Roth), 5·0; OH (Zerewitinoff in anisole), 0·4; NH (temperature raised to 120° after preceding determination), 0·05. $C_{22}H_{28}O_2N_2$ requires C, 74·95; H, 8·0; N, 7·95; OMe, 8·8; CMe, 7·6%]. No acetone distils from alcoholic solutions of *iso*propylideneniquine, but when such solutions are neutralised with aqueous mineral acids, or when the solid base is dissolved in dilute mineral acids, the resulting solutions contain free acetone which can be distilled off. The acetone was detected in the distillate by the Legal nitroprusside test and was isolated as the *p*-nitrophenylhydrazone, m. p. 146—150°, which, when mixed with an authentic specimen, m. p. 150—152°, showed mixed m. p. 147—151°. Such neutralised or acidified solutions of the base contain also free niquine, the salts of which crystallise when these solutions are evaporated. In view of this behaviour of *iso*propylideneniquine in acid solution, it is hardly surprising that its specific rotation in 0·1N-sulphuric acid should be lower than the corresponding figure for niquine very nearly in proportion of the molecular weights of the two bases, but there is no perceptible mutarotation which might have signified hydrolysis during the actual deter-

mination. *iso*Propylideneniquine in alcoholic solution absorbs one molecule of hydrogen in presence of Adams's platinic oxide catalyst, but the product has not been isolated; when neutralised, the reduced solution furnishes salts of dihydroniquine. An attempt to prepare "methyleneniquine" by heating niquine (2 g.) with 40% aqueous formaldehyde (20 c.c.) in a sealed tube at 95—105° for 7 hours furnished an amorphous, ether-soluble base (1·46 g.), which in alcoholic solution absorbed 117 c.c. of hydrogen in presence of Adams's platinic oxide catalyst. The reduced compound was itself amorphous, and was expected, by analogy, to furnish on neutralisation salts of dihydroniquine. Unlike the latter, however, the substance would not crystallise as hydrochloride, sulphate, or dihydrobromide.

Dihydroniquine (IV; R = $CH_3 \cdot CH_2 \cdot CH_2$) was prepared by hydrogenating a solution of niquine (10 g.) in 5% hydrochloric acid (200 c.c.) in the presence of Adams's platinic oxide catalyst (0·1 g.). The reduction proceeded rapidly, particularly if the niquine solution was first filtered through kieselguhr, and was complete in 3 hours. After removal of the catalyst, the base was discharged to ether by sodium hydroxide solution; it crystallised from ether in tufts of soft, feathery needles, which sintered at 50°, became translucent at 65°, and gradually melted to a colourless oil at 85°. The needles, $[\alpha]_D^{16°}$ — 210·1° (0·1N-sulphuric acid), contain $1·5H_2O$, which can be expelled in a vacuum over sulphuric acid, $1H_2O$ being re-absorbed on exposure (Found: C, 72·1; H, 8·2; N, 8·7. $C_{19}H_{26}O_2N_2$ requires C, 72·6; H, 8·3; N, 8·9%). The *hydrochloride* crystallises from water in colourless, brittle needles, m. p. 185°, $[\alpha]_D$ — 190° to — 192° (0·1N-hydrochloric acid), sparingly soluble in water, more easily in alcohol (Found: loss at 110° in a vacuum, 3·7—4·2. $C_{19}H_{26}O_2N_2,HCl,H_2O$ requires H_2O, 4·9%. Found in salt so dried: C, 64·5; H, 8·0; N, 7·95; Cl, 10·1. $C_{19}H_{26}O_2N_2,HCl$ requires C, 65·0; H, 7·8; N, 8·0; Cl, 10·1%). The *sulphate* crystallises from aqueous alcohol or from water in colourless feathery needles, m. p. 172° (decomp.) after softening, and seems to have the composition $B_2,2H_2SO_4$. It is sparingly soluble in alcohol and very sparingly in water. Its water content is variable, and drying figures at temperatures ranging from 100° to 150° in a vacuum include 7·45 as a minimum, and 16·3% as a maximum, corresponding to $B_2,2H_2SO_4,5H_2O$ and $B_2,2H_2SO_4,12·5H_2O$ respectively (Found in anhydrous salt: C, 59·85; H, 7·3; N, 7·45. $3C_{19}H_{26}O_2N_2,2H_2SO_4$ requires C, 60·1; H, 7·25; N, 7·4%). No satisfactory sulphur values could be obtained. The acid oxalate crystallises from aqueous alcohol in faintly pink needles, m. p. 207° after sintering at 180°. The dihydrobromide crystallises from water in tiny, brittle, anhydrous needles, m. p. 248° (decomp.) after darkening from about 210° onwards, $[\alpha]_D^{15°}$ — 134·5°, — 137·9° (water). *Nitrosodihydroniquine* was prepared by cooling in ice a solution of dihydroniquine hydrochloride (0·5 g.) in dilute hydrochloric acid (20 c.c.) and adding a large excess of a concentrated solution of sodium nitrite. An oil formed, which crystallised on standing (0·49 g.). This nitroso-nitrate, which crystallised from alcohol in circular sheaves of fine colourless needles and was very sparingly soluble in water, was dissolved in alcohol and treated with aqueous sodium hydroxide; the solution was evaporated to low bulk and extracted with ether. The aqueous liquor gave the reactions of nitrate but not of nitrite, showing that dihydroniquine, like niquine, gives with nitrous acid the nitroso-nitrate and not the nitroso-nitrite or hydrochloride (compare Skraup). The ethereal extract deposited on concentration transparent, anhydrous, almost colourless, irregular plates, m. p. 131° (Found: C, 66·4; H, 7·5; N, 12·0. $C_{19}H_{25}O_2N_3$ requires C, 66·4; H, 7·3; N, 12·2%).

N-*Methyldihydroniquine*.—A warm, two-phase mixture of a solution of dihydroniquine (26 g.) in ether (600 c.c.) and 10% sodium carbonate solution (105 c.c.) was shaken for 2 hours with methyl sulphate (11 g.). The golden-brown ethereal layer was washed with alkalised water and refluxed with charcoal; it then furnished a crystalline residue (19 g.), which was recrystallised from acetone (35 c.c.)–petroleum (b. p. 60—80°; 100 c.c.). This *base* (17·5 g.) separated from acetone in silky, colourless needles, m. p. 121°, $[\alpha]_D^{15°}$ — 227·3° (0·1N-hydrochloric acid) or — 169·9° (alcohol) (Found: loss at 95° in a vacuum, 4·9. Found for the base so dried: C, 73·0; H, 8·6; N, 8·3; OMe, 9·8; NMe, 8·2. $C_{20}H_{28}O_2N_2,H_2O$ requires H_2O, 5·2%. $C_{20}H_{28}O_2N_2$ requires C, 73·15; H, 8·6; N, 8·5; OMe, 9·45; NMe, 8·8%). The *tartrate* crystallised from acetone in felted needles, m. p. 134—136°, $[\alpha]_D^{17°}$ — 113·1° (water) (Found: loss at 90° in a vacuum, 3·4. Found for the salt so dried: C, 65·2; H, 7·8; N, 6·9. $2C_{20}H_{28}O_2N_2,C_4H_6O_6,1·5H_2O$ requires H_2O, 3·2%. $2C_{20}H_{28}O_2N_2,C_4H_6O_6$ requires C, 65·5; H, 7·75; N, 6·9%). The methiodide crystallised from acetone in tiny, fawn-coloured, granular masses of needles, m. p. 216—218° (decomp.).

Epimerisation of Dihydroniquine by Boiling Dilute Acetic Acid.—Dihydroniquine hydrochloride (5 g.) was refluxed with 10% acetic acid (55 c.c.) for 24 hours. The basic product (4·4 g.), discharged to ether by sodium hydroxide solution, was an optically inactive, brown oil,

which gave no reaction for cinchonatoxins with the sodium nitroprusside reagent of Bachstez and Caro (*loc. cit.*); it contained dihydroniquidine and *epi*-C_9-dihydroniquidine (see Part VI). The former was isolated as crude acid oxalate by converting the total product into that salt and crystallising it from water as far as possible. The uncrystallisable mother-liquors, containing about two-thirds of the original material, were then worked up for base and converted into acid hydrobromide in aqueous solution. Crude *epi*-C_9-dihydroniquidine sesquihydrobromide (see Part VI) separated, and after recovery of as much as would crystallise, there was left about one-third of the original material, and this would not crystallise as oxalate, hydrobromide, hydrochloride, or tartrate.

Dihydroniquidine from Epimerisation of Dihydroniquine.—From the crops of dihydroniquidine acid oxalate obtained above, the base was recovered and crystallised several times from ether and from acetone. It had m. p. and mixed m. p. 166—168°, $[\alpha]_D^{17°}$ + 230·2° (0·1N-hydrochloric acid), and $[\alpha]_D^{20°}$ + 124·8° (alcohol). [The corresponding figures given in Part VI for this substance as obtained from quinidine *via* niquidine were m. p. 165°, $[\alpha]_D^{18°}$ + 231·6° (0·1N-sulphuric acid), and $[\alpha]_D^{18°}$ + 126·8° (*c* = 1 in alcohol)] (Found: C, 72·25; H, 8·2; N, 8·9; OMe, 9·6. Calc. for $C_{19}H_{26}O_2N_2$: C, 72·6; H, 8·3; N, 8·9; OMe, 9·9%). The *hydrochloride* has m. p. 238° and $[\alpha]_D^{22°}$ + 206·3° (0·1N-hydrochloric acid) (Found: loss at 115° in a vacuum, 7·0. Found for the substance so dried: C, 64·65; H, 7·85; N, 7·7; Cl, 10·0; OMe, 8·5. $C_{19}H_{26}O_2N_2$,HCl,1·5H_2O requires H_2O, 7·15%. $C_{19}H_{26}O_2N_2$,HCl requires C, 65·0; H, 7·8; N, 8·0; Cl, 10·1; OMe, 8·8%). The acid oxalate crystallises from water or alcohol in tiny apricot-coloured needles, m. p. 189—191° after sintering at 165°. It is fairly readily soluble in water.

epi-C_9-*Dihydroniquidine from Epimerisation of Dihydroniquine.*—The crude substance, obtained above as sesquihydrobromide, was repeatedly recrystallised from water. The identity of the *epi*-C_9-dihydroniquidine so obtained with that prepared by the epimerisation of dihydroniquidine and described in Part VI, is apparent from the following table.

epi-C_9-*Dihydroniquidine.*

Derivative.	From dihydroniquine; or found (analytical figures).	From dihydroniquidine; quoted from Part VI, or calc. (analytical figures).
Base:	Oil:	Glass:
	$[\alpha]_D^{17°}$ −132° (0·1N-sulphuric acid)	$[\alpha]_D^{18°}$ −140·8° (0·1N-sulphuric acid)
Sesquihydrobromide	Felted needles from water, m. p. 241° (decomp.) with previous darkening, mixed m. p. 237°	Silky needles from 50% alcohol; B_2,3HBr,H_2O, m. p. 240°
	$[\alpha]_D^{18°}$ −106·0° (0·1N-sulphuric acid)	$[\alpha]_D^{18°}$ −102·8° (0·1N-sulphuric acid)
	Loss at 110° in a vacuum, 2·0%	Calc. for $(C_{19}H_{26}O_2N_2)_2$,3HBr,H_2O: H_2O, 2·1%
	C, 51·7; H, 6·4; N, 6·5; Br, 27·45; OMe, 7·15%	Calc. for $(C_{19}H_{26}O_2N_2)_2$,3HBr: C, 52·4; H, 6·4; N, 6·4; Br, 27·5; OMe, 7·1%
Sesquinitrate	Rosettes of needles from aqueous alcohol, m. p. 205° (decomp.), mixed m. p. 201°	Clusters of needles from alcohol, B_2,3HNO_3,2H_2O, m. p. 196° (decomp.). [On taking the m. p. of this specimen, 203° (decomp.) is now recorded]
	$[\alpha]_D^{17°}$ −113° (0·1N-sulphuric acid)	$[\alpha]_D^{18°}$ −110·3° (0·1N-sulphuric acid)
	Loss at 120° in a vacuum, 4·3%	Calc. for $(C_{19}H_{26}O_2N_2)_2$,3HNO_3,2H_2O: H_2O, 4·5%
	C, 55·7; H, 6·8; N, 11·6%	Calc. for $(C_{19}H_{26}O_2N_2)_2$,3HNO_3: C, 55·8; H, 6·7; N, 12·0%

Oxidation of Dihydroniquine with Hydrogen Peroxide.—Dihydroniquine (7·1 g.) was heated on a steam-bath with hydrogen peroxide ("90/100 volume"; 35·5 c.c.) for 2 hours. The product consisted of a dark crystalline paste containing much tar under a paler liquor. The latter was decanted, and the tarry paste boiled with water (35 c.c.) for 1 minute. After cooling, the supernatant liquor was decanted into the original one, and this process was repeated. The combined aqueous liquors were treated with sodium hydroxide until they were just alkaline to phenolphthalein, and were then boiled with traces of platinum-black until no further effervescence occurred and they no longer turned potassium iodide–starch paper blue. The vapours were alkaline to litmus. The solution was then nearly neutralised with dilute sulphuric acid, concentrated, and acidified and the crystalline quininic acid (2·43 g.) precipitated was removed (see below). The filtrate was repeatedly extracted with ether; the extracts in the course of concentration deposited a further amount of crude quininic acid (0·23 g.) and finally furnished an oil (2·61 g.); this was dissolved in water, and the solution filtered and evaporated to dry-

ness again (2·52 g.). This crude acid was refluxed for 20 minutes with thionyl chloride (20 c.c.), the mixture evaporated to dryness, and the residue dissolved in benzene and treated with a solution of aniline (3·5 g.) in benzene. The crystalline dianilide of β-propylglutaric acid (2·2 g.) was recrystallised from alcohol, 0·8 g. being obtained, m. p. and mixed m. p. 212—214° (the specimen used for admixture was that stated in Part VII to have m. p. 219°). The crude quininic acid (above) (2·43 g.) was boiled out with alcohol, and the filtrate allowed to crystallise. The crop (1·62 g.) showed m. p. 282°, which, for a mixture with authentic quininic acid (m. p. 296°), rose to 293°.

The author is much indebted to Dr. T. A. Henry for his interest and encouragement, and desires to thank Mr. A. W. Stokes for his considerable share in the experimental work. All the analyses recorded are micro-analyses, for which the author is indebted to Messrs. A. Bennett and H. C. Clarke of the Wellcome Chemical Works, Dartford, Kent.

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20. *The Dehalogenation of 6-Chloro-3-benzoyloxy-Δ⁴-cholestene.*

By F. S. SPRING and G. SWAIN.

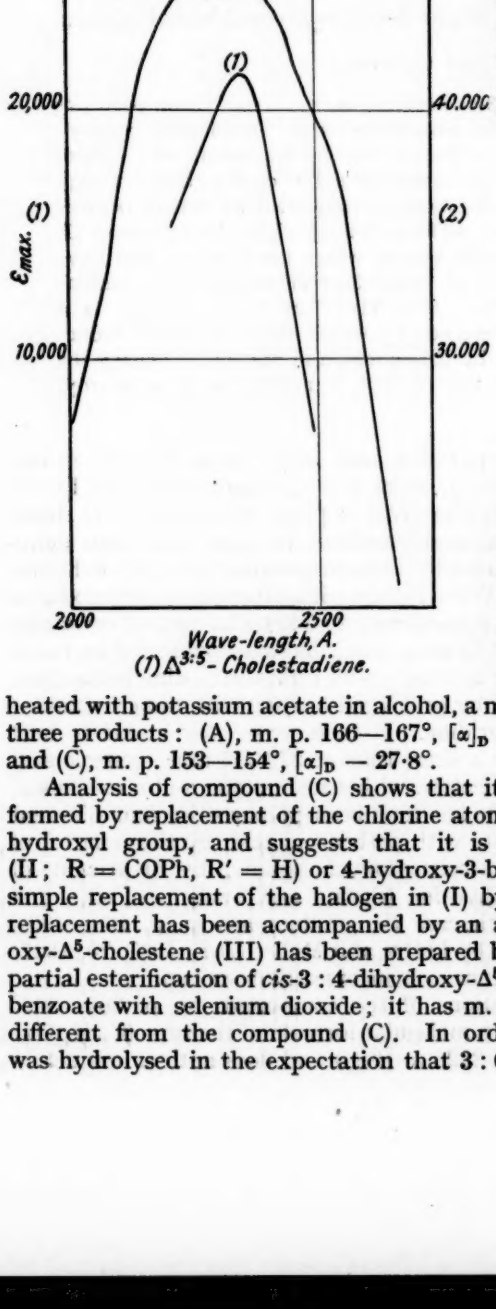
Attempts have been made to dehydrate β-cholesteryl benzoate oxide; on pyrolysis it is isomerised in part with production of the α-benzoate oxide. 6-Chloro-3-benzoyloxy-Δ⁴-cholestene (I), which is obtained from the α-oxide by treatment with hydrochloric acid, when reduced with aluminium amalgam gives Δ³·⁵-cholestadiene in high yield, replacement of the halogen atom having been accompanied by loss of benzoic acid. When treated with potassium acetate, 6-chloro-3-benzoyloxy-Δ⁴-cholestene (I) gives a mixture of three halogen-free products, two of which are isomeric and have been identified as benzoate monoethyl ethers of either 3 : 4-dihydroxy-Δ⁵-cholestene (V) or 3 : 6-dihydroxy-Δ⁴-cholestene (II, R = R′ = H). The third product is a monobenzoate of *cis*-3 : 4-dihydroxy-Δ⁵-cholestene (V), which differs from the monobenzoate of the *cis*-diol previously described by Rosenheim and Starling. During the formation of one of the monobenzoates of the *cis*-diol, a migration of a benzoyl group from C_3 to C_4 has occurred.

WE have previously reported upon the preparation and some properties of α- and β-cholesteryl benzoate oxides (Spring and Swain, J., 1939, 1356), a study instigated by the fact that dehydration of 2-methyl-Δ¹-butene oxide gives isoprene (Kyriakides, *J. Amer. Chem. Soc.*, 1914, **36**, 663); it was hoped that under suitable reaction conditions dehydration of cholesteryl ester oxides would lead either to the corresponding ester of 7-dehydrocholesterol or to that of Δ⁴·⁶-cholestadienol. When heated with either phosphoric oxide or dehydrated alum, α-cholesteryl benzoate oxide is isomerised to 6-ketocholestanyl benzoate; the oxide is stable to prolonged heating at 270°/13 mm., and is likewise unaffected by treatment with thionyl chloride in pyridine and by heating under reflux with dimethylaniline. β-Cholesteryl benzoate oxide also is unaffected by prolonged heating with dimethylaniline and by treatment with thionyl chloride in pyridine. It is, however, less stable to heat treatment than its α-isomer; after heating for a short time at 270°/13 mm., benzoic acid sublimed and the residue was resolved into α-cholesteryl benzoate oxide and a *compound*, m. p. 300—302°. α-Cholesteryl benzoate oxide has now been prepared by four different methods, *viz.*, treatment of cholesteryl benzoate with perbenzoic acid, by the removal of hydrogen chloride from 6-chloro-5-hydroxy-3-benzoyloxycholestane, by treatment of 3 : 5 : 6-trihydroxycholestane with benzoic anhydride (Spring and Swain, *loc. cit.*), and now by isomerisation of the β-oxide. In each case the product has m. p. 168—169°, $[\alpha]_D$ — 31°; the product, m. p. 181°, described by Lettré and Müller (*Ber.*, 1937, **70**, 1947) as α-cholesteryl benzoate oxide is either a mixture or is incorrectly described.

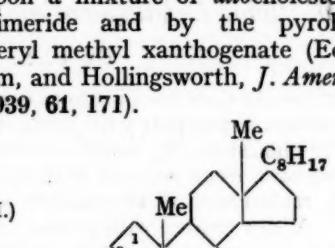
Analysis and molecular weight determinations of the compound, m. p. 300—302° (which is obtained in very small yield), indicate a molecular formula of the type $(C_{27}H_{42}O)_3$. It exhibits an intense absorption maximum at 3825 A. (Fig.) and does not contain active

hydrogen (Zerewitinoff). The amount of this substance available was not sufficient for further examination.

In view of this failure to dehydrate the cholesteryl benzoate oxides in the desired manner, attention was next directed to the removal of hydrogen chloride from 6-chloro-3-benzoyloxy-Δ^4-cholestene (I), previously obtained by us from α-cholesteryl benzoate oxide (*loc. cit.*). In order further to characterise this intermediate it was reduced with aluminium amalgam in moist ether. Instead of the expected *allo*cholesteryl benzoate (3-benzoyloxy-Δ^4-cholestene) a cholestadiene, $C_{27}H_{44}$, m. p. 80—81°, $[\alpha]_D$ — 129·6°, was obtained in high yield. An examination of the spectrum of this hydrocarbon by Dr. A. E. Gillam (to whom we are also indebted for the previously mentioned absorption spectrum) has shown it to possess an intense absorption maximum at 2350 A. (Fig.); the location of the absorption maximum and the strong lævorotation indicate that the hydrocarbon is $\Delta^{3:5}$-cholestadiene (Stavely and Bergmann, *J. Org. Chem.*, 1937, **1**, 567). In physical properties it closely resembles the cholestadienes obtained by the action of hydrochloric acid upon a mixture of *allo*cholesterol and its epimeride and by the pyrolysis of cholesteryl methyl xanthogenate (Eck, Van Peursem, and Hollingsworth, *J. Amer. Chem. Soc.*, 1939, **61**, 171).



(I.)



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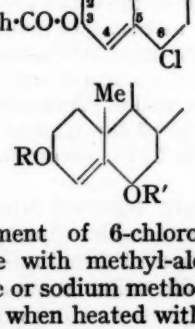


Treatment of 6-chloro-3-benzoyloxy-Δ^4-cholestene with methyl-alcoholic potassium hydroxide or sodium methoxide gave unworkable oils; when heated with pyridine, it gave a chlorine-free resinous product which could not be crystallised. The halogen atom of 6-chloro-3-benzoyloxy-Δ^4-cholestene was successfully removed when the compound was heated with potassium acetate in alcohol, a mixture being obtained which was resolved into three products: (A), m. p. 166—167°, $[\alpha]_D$ — 47·2°; (B), m. p. 131—132°, $[\alpha]_D$ — 29·4°, and (C), m. p. 153—154°, $[\alpha]_D$ — 27·8°.

Analysis of compound (C) shows that it has the formula $C_{34}H_{50}O_3$, that it has been formed by replacement of the chlorine atom of 6-chloro-3-benzoyloxy-Δ^4-cholestene by a hydroxyl group, and suggests that it is either 6-hydroxy-3-benzoyloxy-Δ^4-cholestene (II; R = COPh, R′ = H) or 4-hydroxy-3-benzoyloxy-Δ^5-cholestene (III); in the former, simple replacement of the halogen in (I) by hydroxyl is assumed and in the latter this replacement has been accompanied by an allylic rearrangement. 4-Hydroxy-3-benzoyloxy-Δ^5-cholestene (III) has been prepared by Rosenheim and Starling (J., 1937, 377) by partial esterification of *cis*-3 : 4-dihydroxy-Δ^5-cholestene (V) and by oxidation of cholesteryl benzoate with selenium dioxide; it has m. p. 209—210°, $[\alpha]_D$ — 30·7°, and is markedly different from the compound (C). In order further to characterise compound (C), it was hydrolysed in the expectation that 3 : 6-dihydroxy-Δ^4-cholestene (II; R = R′ = H)

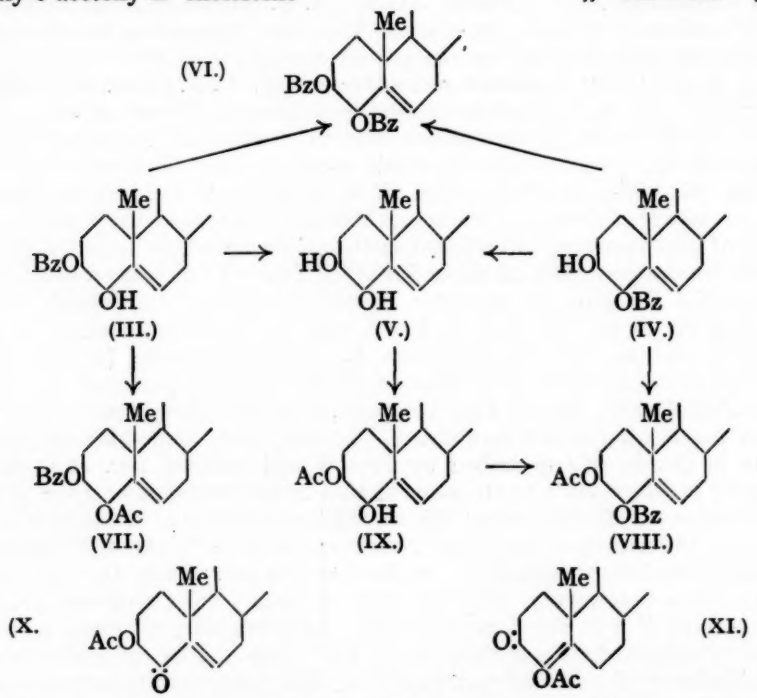
would be obtained; the product proved to be *cis*-3 : 4-dihydroxy-Δ^5-cholestene (V), the identity being established by direct comparison with a specimen prepared by the method of Rosenheim and Starling and also by the preparation of the diacetate, m. p. 168—169°. Benzoylation of compound (C) gave *cis*-3 : 4-dibenzoyloxy-Δ^5-cholestene, m. p. 150—151° (VI). Acetylation, however, gave a *benzoate-acetate*, m. p. 130—131°, differing greatly from the *cis*-3-benzoyloxy-4-acetoxy-Δ^5-cholestene (VII), m. p. 166—167°, described by Rosenheim and Starling. The only feasible explanation of this series of relationships appeared to be that compound (C) is 3-hydroxy-4-benzoyloxy-Δ^5-cholestene (IV), a migration of the benzoyl group from C_3 to C_4 having occurred during its formation; according to this explanation, the benzoate-acetate, m. p. 130—131°, will be 4-benzoyloxy-3-acetoxy-Δ^5-cholestene (VIII). In order to test this explanation, 4-hydroxy-3-acetoxy-Δ^5-cholestene (IX) was prepared by the partial acetylation of the 3 : 4-diol (V) (Petrow and Starling, J., 1940, 60; cf. Marker and Rohrmann, *J. Amer. Chem. Soc.*, 1939, **61**, 3022) and benzoylated; the product, presumably 4-benzoyloxy-3-acetoxy-Δ^5-cholestene (VIII), proved to be identical with the benzoate-acetate, m. p. 130—131°, obtained by acetylation of the compound (C), which accordingly would appear to have the structure (IV).

Reviewing this series of relationships, it is established that two monobenzoates of *cis*-3 : 4-dihydroxy-Δ^5-cholestene exist (m. p.'s 209—210° and 153—154°), which are position isomers and not stereoisomers. The higher-melting isomer has been accorded the 3-benzoate structure (III) on evidence (Rosenheim and Starling, *loc. cit.*) which appears sound: namely, that the 3 : 4-diol (V) gives an insoluble digitonide, whereas the monobenzoate, m. p. 209—210°, fails to do so. We find, however, that the monobenzoate, m. p. 153—154°, likewise fails to give an insoluble digitonide, the conclusions being (*a*) that the presence of a 4-benzoyl group inhibits the formation of an insoluble digitonide in 3-hydroxy-4-benzoyloxy-Δ^5-cholestene, and (*b*) that the position of the ester group in the two monobenzoates of the *cis*-diol is not established. In the same connection we find that the monoacetate of the *cis*-diol described by Petrow and Starling (*loc. cit.*), the esterified hydroxyl group in which must be the same as that in the monobenzoate, m. p. 209—210°, does not give an insoluble digitonide; the second monoacetate of the *cis*-diol is unknown. The reactions of the monoacetate of the *cis*-diol described by Petrow and Starling (*loc. cit.*) have been interpreted by these authors on the then fair assumption that it is the 3-monoacetate (IX). It is noteworthy, however, that an equally valid representation of the reactions is obtained if it is the 4-monoacetate. In particular, reference is made to the intermediate unsaturated keto-acetate, m. p. 124°, obtained by bromination, oxidation, and debromination of the *cis*-diol monoacetate. This compound is formulated as 3-acetoxy-Δ^5-cholesten-4-one (X), a constitution stated to be in conformity with its ultra-violet absorption spectrum, which shows a band at 2800 A. By all analogies the simple $\alpha\beta$-unsaturated ketone (X) would be expected to exhibit an absorption maximum in the region 2300—2500 A. If the monoester is the 4-monoacetate, the intermediate unsaturated keto-acetate must be 4-acetoxy-Δ^4-cholesten-3-one (XI), *i.e.*, a simple diosphenol derivative, a structure which, although in harmony with the formation of cholestane-3 : 4-dione by hydrolysis, is still difficult to reconcile with the light absorption properties, since the mono-enol acetate, m. p. 100—101°, prepared from cholestane-3 : 4-dione by treatment with acetic anhydride exhibits an absorption maximum between 2400 and 2500 A. (Butenandt, *Ber.*, 1936, **69**, 2779) and the mono-enol acetates similarly prepared from forms (A) and (B) of cholestane-2 : 3-dione exhibit absorption maxima at 2380 and 2370 A., respectively (Stiller and Rosenheim, J., 1938, 353). The conversion of the monoacetate of the *cis*-diol into 4-acetoxy-$\Delta^{4:6}$-cholestadien-3-one would be more simply explained if the former is the 4-monoester. However, it must be stressed that evidence of this nature is not conclusive, and for the time being the orientation of the monoesters of *cis*-3 : 4-dihydroxy-Δ^4-cholestene must be considered as not rigidly established.

Analyses of the two products (A) and (B) indicate that they are isomers of the formula $C_{36}H_{54}O_3$ and that each contains an ethoxyl group. This evidence and a consideration of their origin suggest that they are to be formulated as ester-ethers of either *cis*-3 : 4-dihydroxy-Δ^5-cholestene or 3 : 6-dihydroxy-Δ^4-cholestene. In view of the possibility of migration of the benzoyl group there are four probable structures for compounds (A) and

(B). Hydrolysis of compound (A) gives a ***diol monoethyl ether***, m. p. 123—124°, $[\alpha]_D$ — 59·2°, characterised by the preparation of the ***diol monoethyl ether-acetate***, m. p. 120—121°, $[\alpha]_D$ — 83·5°. Hydrolysis of compound (B) gives a ***diol monoethyl ether***, m. p. 122—123° [which differs from the isomer obtained from compound (A)], characterised as its ***acetate***, m. p. 150°. A similarity is to be observed in the physical properties of compound (B) and 3-benzoyloxy-6-acetoxy-Δ^4-cholestene (Rosenheim and Starling, *loc. cit.*; Petrow, Rosenheim, and Starling, J., 1938, 677):

Compound (B)	m. p. 131—132° $[\alpha]_D$ — 29·4°
3-Benzoyloxy-6-acetoxy-Δ^4-cholestene	„ 128—129° „ — 21·2°



This similarity is, moreover, accentuated by the fact that a mixture of the two does not exhibit a melting point depression. This coincidence suggested that compound (B) is 3-benzoyloxy-6-ethoxy-Δ^4-cholestene, formed by direct replacement of the chlorine in (I) by an ethoxyl group. This view, however, is not supported by the fact that the hydrolysis product (diol monoethyl ether) of substance (B) does not give a digitonide. A similar behaviour is observed in the case of the diol monoethyl ether obtained by hydrolysis of substance (A).

Experimental.

Optical rotations were measured in chloroform solution in a 1-dm. tube.

Pyrolysis of β-Cholesteryl Benzoate Oxide.—The oxide (m. p. 151—152°; 10 g.) was heated at 270°/13 mm. for 30 minutes. A sublimate of benzoic acid (1·1 g.) was collected and the residual opaque yellow resin was taken up in hot ethyl acetate (50 c.c.). The crystalline deposit obtained on cooling was recrystallised from ethyl acetate and then from chloroform–ethyl acetate (1 : 1), from which the *compound* (0·2 g.) separated in small yellow needles, m. p. 300—302° (decomp.), $[\alpha]_D^{22°}$ — 16·5° ($c = 1·2$). The compound is readily soluble in chloroform, sparingly soluble in ethyl acetate, and insoluble in alcohol and light petroleum; it gives an intense cherry-red coloration with antimony trichloride in chloroform [Found: C, 85·1, 84·5; H, 11·2, 11·5; *M*, 1160 (Rast), 1110 (Rieche). $(C_{27}H_{42}O)_3$ requires C, 84·7; H, 11·1%; *M*, 1148].

Concentration of the ethyl acetate mother-liquor gave a crystalline solid (3 g.), m. p. 150—153°, which after three crystallisations from ethyl acetate gave α-cholesteryl benzoate oxide,

m. p. 168—169°, undepressed when mixed with an authentic specimen. Hydrolysis with methyl-alcoholic potassium hydroxide gave α-cholesterol oxide, m. p. 140—141°, undepressed when mixed with an authentic specimen.

Cholestadiene.—A solution of 6-chloro-3-benzoyloxy-Δ^4-cholestene (1 g.) in ether (150 c.c.) was added to aluminium amalgam prepared from aluminium foil (5 g.) as described by Vogel (J., 1927, 594). The mixture was set aside at room temperature for 45 hours, with occasional additions of small amounts of water. The liquid was then filtered and washed with water, and the ether removed from the dried solution. After one crystallisation from ethyl acetate the product (0·8 g.) had m. p. 78—79° and after two further crystallisations from ethyl acetate–methyl alcohol (3 : 1) it gave cholestadiene in long prismatic needles, m. p. 80—81°, $[\alpha]_D^{20°}$ — 129·6° (c = 2·9). It gave an intense orange coloration with tetranitromethane in chloroform and, with antimony trichloride in chloroform, an orange, changing to cherry-red on standing (Found : C, 87·9; H, 12·0. Calc. for $C_{27}H_{44}$: C, 88·0; H, 12·0%).

Treatment of 6-*Chloro*-3-*benzoyloxy*-Δ^4-*cholestene with Potassium Acetate in Alcohol. Compound* (*A*).—6-Chloro-3-benzoyloxy-Δ^4-cholestene (10 g.) was refluxed for 8 hours with freshly fused potassium acetate (40 g.) and absolute alcohol (400 c.c.). The mixture was diluted with water and extracted with ether. The extract was washed with water and dried (sodium sulphate), and the solvent removed. The colourless resin obtained was taken up in hot ethyl acetate (20 c.c.) and methyl alcohol (7 c.c.). The crystalline solid separating on standing (1·1 g.; m. p. 145—155°) was twice crystallised from ethyl acetate–methyl alcohol (4 : 1), from which the *diol monoethyl ether benzoate* (compound A) separated in plates, m. p. 166—167° (const.), $[\alpha]_D^{20°}$ — 47·2° (c = 0·85). It was readily soluble in chloroform and hot ethyl acetate but sparingly soluble in alcohol and gave an intense violet coloration with antimony trichloride in chloroform. A mixture with 3-benzoyloxy-4-acetoxy-Δ^5-cholestene, m. p. 166—167° (for which we are indebted to Dr. O. Rosenheim), melted at 155—157° (Found : C, 80·6; H, 10·3; OEt, 8·5. $C_{36}H_{54}O_3$ requires C, 80·85; H, 10·2; OEt, 8·4%).

Diol Monoethyl Ether.—Compound (A) (0·2 g.) was refluxed for 3 hours with methyl-alcoholic potassium hydroxide (20 c.c.; 3%). The crystalline solid separating on cooling was recrystallised from methyl alcohol, yielding the *diol monoethyl ether* in blades, m. p. 123—124°, $[\alpha]_D^{20°}$ — 59·2° (c = 0·76). With the antimony trichloride reagent a pink colour developed after about 1 minute; the diol ether gave a weak yellow coloration with tetranitromethane in chloroform (Found : C, 80·5; H, 11·4; OEt, 11·3. $C_{29}H_{50}O_2$ requires C, 80·9; H, 11·7; OEt 10·5%).

Diol Monoethyl Ether Acetate.—The diol monoethyl ether (0·3 g.) was refluxed for 1 hour with acetic anhydride (2 c.c.) and pyridine (2 c.c.). The product, isolated by the addition of water, was crystallised from ethyl acetate–methyl alcohol (1 : 2), from which the *diol monoethyl ether acetate* separated in plates, m. p. 120—121°, $[\alpha]_D^{20°}$ — 83·5° (c = 2·1). It gave an intense red-violet coloration with the antimony trichloride reagent (Found : C, 78·4; H, 11·4. $C_{31}H_{52}O_3$ requires C, 78·8; H, 11·1%).

Compound (*B*).—Concentration of the original ethyl acetate–methyl alcohol mother-liquor obtained after removal of the crude compound (A) (m. p. 144—155°) gave a crystalline solid (4·8 g.). This was fractionally crystallised from ethyl acetate–methyl alcohol. The top crop was repeatedly crystallised from the same solvent mixture, giving the *diol monoethyl ether benzoate* (compound B) (0·8 g.) in needles, m. p. 131—132°, $[\alpha]_D^{20°}$ — 29·4° (c = 1·2). It was readily soluble in chloroform, less so in ethyl acetate, and sparingly soluble in alcohol. With the antimony trichloride reagent it gave a violet solution. The m. p. of compound (B) is not depressed when this is mixed with 3-benzoyloxy-6-acetoxy-Δ^4-cholestene (m. p. 128—129°) (kindly supplied by Dr. O. Rosenheim) (Found : C, 80·8; H, 10·1; OEt, 8·1. $C_{36}H_{54}O_3$ requires C, 80·85; H, 10·2; OEt, 8·4%).

Diol Monoethyl Ether.—The above benzoate (0·5 g.) was refluxed for 1½ hours with methyl-alcoholic potassium hydroxide (40 c.c.; 2½%). The product was isolated by the addition of water, washed, and crystallised from methyl alcohol, from which the *diol monoethyl ether* separated in needles, m. p. 107—108°. After drying in a vacuum over phosphoric oxide at 78° for 6 hours, the compound melted sharply at 122—123°. A mixture with the diol monoethyl ether (m. p. 123—124°) obtained by hydrolysis of compound (A) melted at 100°. With the antimony trichloride reagent the new diol ether gave a violet coloration and with tetranitromethane in chloroform a pale yellow solution (Found : C, 80·6; H, 11·6; OEt, 10·6. $C_{29}H_{50}O_2$ requires C, 80·9; H, 11·7; OEt, 10·5%).

The diol monoethyl ether (0·2 g.) was refluxed for 1 hour with pyridine (1·5 c.c.) and acetic anhydride (1·5 c.c.). The crystalline solid separating on cooling was recrystallised from ethyl acetate–methyl alcohol (1 : 1), from which the *diol monoethyl ether acetate* separated in prismatic

needles, m. p. 150°. It gave a violet coloration with the antimony trichloride reagent (Found : C, 78·3; H, 11·05. $C_{31}H_{52}O_3$ requires C, 78·8; H, 11·1%).

Monobenzoate of cis-3 : 4-*Dihydroxy*-Δ^5-*cholestene* (*Compound C*).—Concentration of the ethyl acetate–methyl alcohol mother-liquor obtained after removal of the top crop (above), followed by repeated crystallisation of the product from the same solvent mixture (2 : 3), gave the *monobenzoate* of the *cis*-diol (1·5 g.) in leaflets, m. p. 153—154°, $[\alpha]_D^{20°}$ − 27·8° (*c* = 1·8). This gave a pink coloration with the antimony trichloride reagent and a yellow coloration with tetranitromethane in chloroform (Found : C, 80·8; H, 10·0. $C_{34}H_{50}O_3$ requires C, 80·6; H, 9·9%). When it was treated in warm alcoholic solution with a solution of digitonin (1% in 90% alcohol), no separation of a digitonide occurred. Under the same (standard) conditions, cholesterol and *cis*-3 : 4-dihydroxy-Δ^5-cholestene gave immediate precipitates of the corresponding digitonides.

The diol monobenzoate (0·5 g.) was refluxed for 1½ hours with methyl-alcoholic potassium hydroxide (3%; 20 c.c.). The product was crystallised from methyl alcohol, giving *cis*-3 : 4-dihydroxy-Δ^5-cholestene in blades, m. p. 175°, $[\alpha]_D^{20°}$ − 61·5° (*c* = 1·7); the m. p. was not depressed by the 3 : 4-diol, m. p. 175—176°, prepared by hydrolysis of 4-hydroxy-3-benzoyloxy-Δ^5-cholestene, m. p. 209—210° (prepared as described by Rosenheim and Starling, *loc. cit.*). Rosenheim and Starling give m. p. 176—177°, $[\alpha]_D$ − 60·0° for the *cis*-3 : 4-diol. Acetylation of the *cis*-3 : 4-diol, m. p. 175°, gave *cis*-3 : 4-diacetoxy-Δ^5-cholestene in needles, m. p. 168—169°, $[\alpha]_D^{20°}$ − 97·4° (*c* = 1·3) (Found : C, 76·6; H, 10·35. Calc. for $C_{31}H_{50}O_4$: C, 76·5; H, 10·4%); the m. p. was not depressed by the diacetate, m. p. 168—169°, obtained from the diol, m. p. 175—176°. Rosenheim and Starling give m. p. 169—170°, $[\alpha]_D$ − 96·1° for the *cis*-3 : 4-diacetate.

cis-3 : 4-*Dibenzoyloxy*-Δ^5-*cholestene*.—The monobenzoate, m. p. 153—154° (0·5 g.), was heated on the steam-bath for 30 minutes with pyridine (5 c.c.) and benzoyl chloride (5 c.c.). The mixture was diluted with sodium carbonate solution (10%) and extracted with ether. The product was crystallised from ethyl acetate–methyl alcohol (1 : 1), from which the dibenzoate separated in needles, m. p. 150—151°, not depressed by a specimen prepared by the method of Rosenheim and Starling (*loc. cit.*) but depressed to 130° by the monobenzoate, m. p. 153—154°.

Benzoate-acetate of cis-3 : 4-*Dihydroxy*-Δ^5-*cholestene*.—(a) The monobenzoate of the *cis*-diol (m. p. 153—154°; 0·3 g.) was refluxed for 1½ hours with pyridine (2 c.c.) and acetic anhydride (2 c.c.). Water was added to the cooled solution, and the crystalline deposit recrystallised from ethyl acetate–methyl alcohol (1 : 1), from which the benzoate-acetate separated in fine needles, m. p. 130—131° (const.), $[\alpha]_D^{20°}$ − 54·8° (*c* = 1·2). It gave an intense violet coloration with antimony trichloride in chloroform (Found : C, 78·5; H, 9·8. $C_{36}H_{52}O_4$ requires C, 78·7; H, 9·6%). Hydrolysis of this compound by the method described for the parent diol monobenzoate gave *cis*-3 : 4-dihydroxy-Δ^5-cholestene, m. p. 175° either alone or when mixed with an authentic specimen, m. p. 175—176°.

(b) The monoacetate of the *cis*-diol (Petrow and Starling, *loc. cit.*) (0·3 g.) was heated on the steam-bath for 1 hour with benzoyl chloride (3 c.c.) and pyridine (3 c.c.). The product, isolated in the usual manner, was twice crystallised from methanol, from which the benzoate-acetate separated in fine needles, m. p. 129—130°, $[\alpha]_D^{20°}$ − 54·4° (*c* = 1·7), not depressed by the specimen prepared by method (a).

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21. *The Properties of* 3 : 6-*Anhydroglucose.*

By W. N. HAWORTH, L. N. OWEN, and F. SMITH.

This work shows that in 3 : 6-anhydroglucose and its derivatives the 3 : 6-anhydro ring acquires the character of the principal ring to which the pyranose and furanose ring is subsidiary. The 3 : 6-anhydro ring governs the structure of these substances and appears to be mainly responsible for their peculiar properties. For example, the α- and the β-form of 3 : 6-anhydromethylglucopyranoside can be directly converted into the more stable 3 : 6-anhydro-α- and -β-methylglucofuranoside respectively; this ring change from pyranoside to furanoside occurs without loss of the glycosidic methyl

residue. Direct transformation of 2 : 4-dimethyl 3 : 6-anhydro-α-methylglucopyranoside into the β-pyranoside has also been effected without loss of the glycosidic methyl group. This change is analogous to that which has been observed to take place in the corresponding compound of the galactose series. It is important to note that such remarkable changes do not occur in the case of pyranosides and furanosides which contain no anhydro ring.

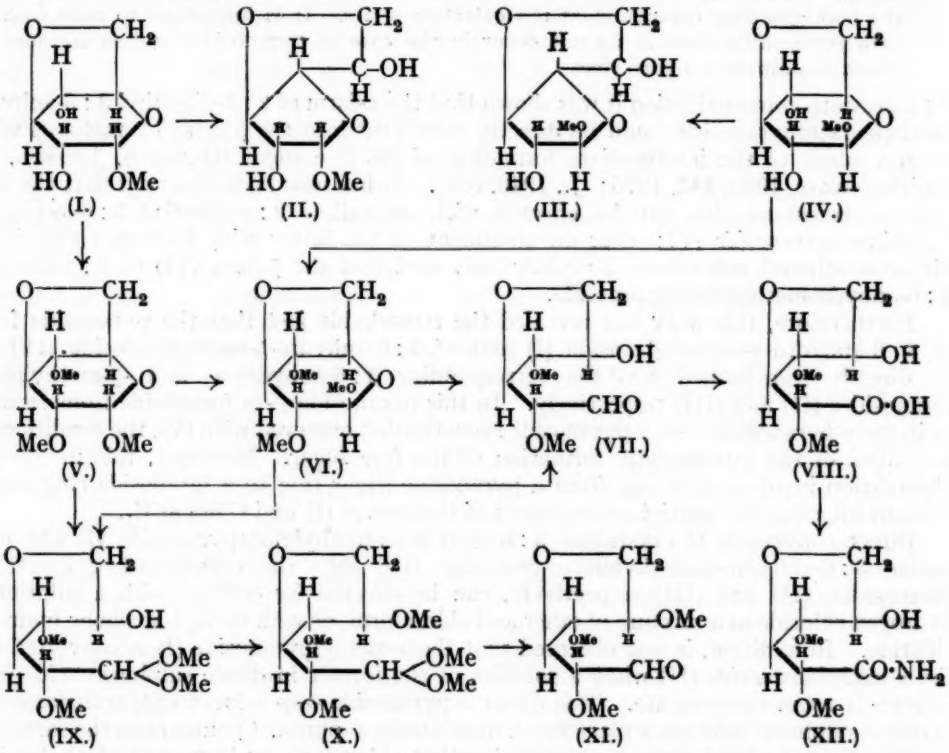
In a previous communication it was shown that the α-form of 2 : 4-dimethyl 3 : 6-anhydromethylgalactopyranoside could be directly converted into the β-form by methods which do not admit of the intermediate formation of the free sugar (Haworth, Jackson, and Smith, *Nature*, 1938, **142**, 1075; J., 1940, 620). It has now been observed that the same type of transformation can be effected with crystalline 2 : 4-*dimethyl* 3 : 6-*anhydro-α-methylglucopyranoside* (V); thus on treatment of the latter with hydrogen chloride in air or in ethereal solution it is rapidly converted into the β-*form* (VI) of 2 : 4-dimethyl 3 : 6-anhydromethylglucopyranoside.

Furthermore, this work has revealed the remarkable fact that the pyranoside forms of 3 : 6-anhydro-α-methylglucoside (I) and of 3 : 6-anhydro-β-methylglucoside (IV) can be directly transformed into the corresponding 3 : 6-anhydro-α- and -β-methylglucofuranosides (II) and (III) respectively. In this pyranoside ⟶ furanoside isomerisation, as in the α-pyranoside ⟶ β-pyranoside isomerisation observed with (V), the conditions do not allow of the intermediate formation of the free sugar. Moreover, this unexpected observation involves a change from a pyranoside sugar ring to a furanoside ring system without affecting the spatial arrangement of the groups (H and OMe) at C_1.

Direct conversion of crystalline 3 : 6-anhydro-α-methylglucopyranoside (I) and crystalline 3 : 6-anhydro-β-methylglucopyranoside (IV) into the corresponding crystalline furanosides, (II) and (III) respectively, can be effected by contact with a solution of hydrogen chloride in a mixture of ether and chloroform, or with methyl-alcoholic hydrogen chloride. In addition, it was observed that the α-methylpyranoside (I) is converted into the α-*methylfuranoside* (II) when a solution of the former in dilute sulphuric acid (0·1N) is kept at room temperature. This direct α-pyranoside ⟶ α-furanoside transformation in dilute sulphuric acid takes place much more slowly (approx. 4 hours) than the same conversion effected with hydrogen chloride in ether–chloroform or in methyl alcohol, which is almost instantaneous in both cases. Nevertheless, the fact emerges that despite the relatively slow rate of isomerisation in aqueous solution, the conversion is accompanied by only slight hydrolysis of the glycosidic methyl group. The reaction follows a different course when the β-methylpyranoside (IV) is treated with dilute sulphuric acid, for in this case hydrolysis occurs slowly with the formation of 3 : 6-anhydroglucose; no 3 : 6-anhydro-β-methylglucofuranoside appears to be formed.

The view expressed concerning the direct conversion of 2 : 4-dimethyl 3 : 6-anhydro-α-methylglucopyranoside (V) into the corresponding β-methylglucopyranoside (VI) is based upon the following experimental facts. Treatment of 6-tosyl α-methylglucopyranoside with a solution of sodium hydroxide results in the formation of 3 : 6-anhydro-α-methylglucopyranoside (I). By similar treatment with sodium hydroxide, β-methylglucopyranoside 6-bromohydrin, obtained from acetodibromoglucose (Fischer and Armstrong, *Ber.*, 1902, **35**, 833), affords 3 : 6-anhydro-β-methylglucopyranoside (IV) (cf. Fischer and Zach, *Ber.*, 1912, **45**, 456). Methylation of (I) with Purdie's reagents yields the crystalline 4-*methyl* 3 : 6-*anhydro-α-methylglucopyranoside* (XXV), which, on further methylation, gives rise to crystalline 2 : 4-*dimethyl* 3 : 6-*anhydro-α-methylglucopyranoside* (V). Similarly, methylation of (IV) with Purdie's reagents furnishes 2 : 4-*dimethyl* 3 : 6-*anhydro-β-methylglucopyranoside* (VI). The crystalline α-isomeride (V), even when kept in a sealed tube at room temperature, gradually changes into the liquid β-form (VI). The same change takes place more rapidly when (V) is exposed to the air, an effect which may be due to traces of acid, to which the compound is extremely sensitive. As previously stated, brief contact with hydrogen chloride in air or with a solution of hydrogen chloride in ether effects this α-pyranoside ⟶ β-pyranoside isomerisation almost instantaneously. Although both the α- and the β-form of 2 : 4-dimethyl 3 : 6-anhydroglucopyranoside undergo hydrolysis at room temperature with 0·1N-sulphuric acid, the β-form is more

slowly hydrolysed than the α-form. In each case there is produced 2 : 4-*dimethyl* 3 : 6-*anhydroglucose*, a liquid which reduces Fehling's solution, decolourises neutral potassium

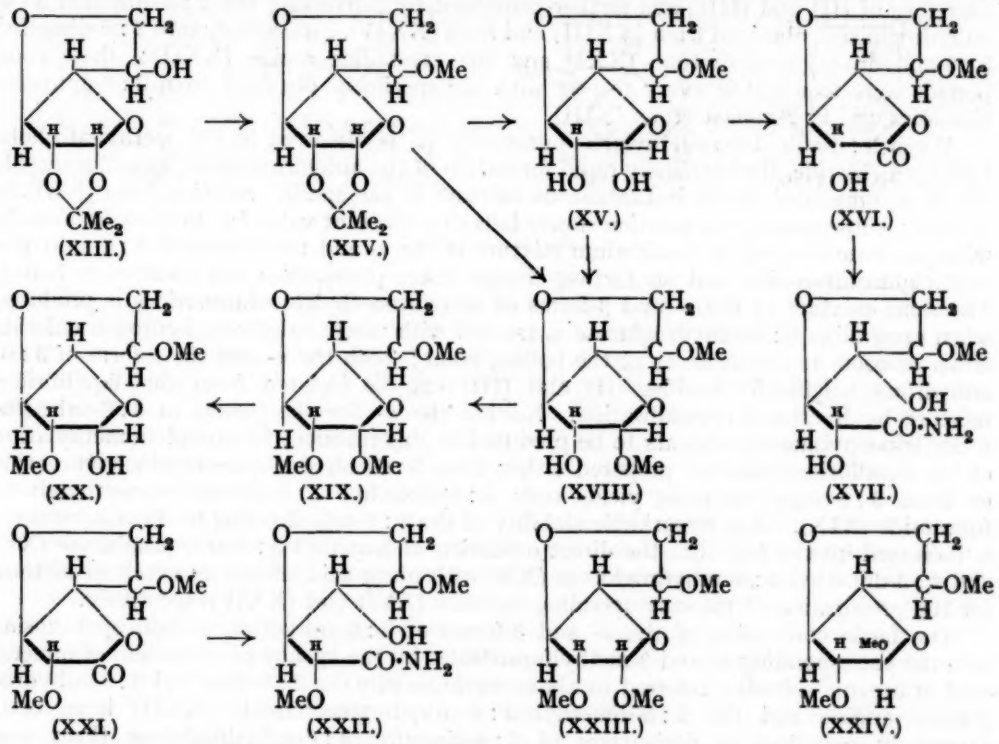


permanganate solution, and restores the colour to Schiff's reagent. Such properties suggest that the 2 : 4-dimethyl 3 : 6-anhydroglucose possesses the aldehydic structure shown in (VII). Oxidation of (VII) with bromine gives crystalline 2 : 4-*dimethyl* 3 : 6-*anhydrogluconic acid* (VIII); the latter is stable in aqueous solution, displays no mutarotation, sublimes unchanged in a vacuum, and shows no tendency to form a lactone. Esterification of (VIII) with diazomethane furnishes the *methyl* ester of 2 : 4-dimethyl 3 : 6-anhydrogluconic acid, which is readily identified by its conversion with methyl-alcoholic ammonia into the corresponding crystalline *amide* (XII).

When 2 : 4-dimethyl 3 : 6-anhydromethylglucopyranoside is treated with an excess of methyl-alcoholic hydrogen chloride at room temperature, it behaves in the same way as the α- and β-forms of 2 : 4-dimethyl 3 : 6-anhydromethylgalactopyranoside, *i.e.*, fission of the 1 : 5-pyranose ring occurs with the formation of 2 : 4-*dimethyl* 3 : 6-*anhydroglucose dimethylacetal* (IX). The only difference noted is that in the galactose series the transformation of the glycosides into the acetal proceeds further towards completion than in the glucose series. The open-chain character of (IX) is demonstrated by the fact that on further methylation with Purdie's reagents it yields 2 : 4 : 5-*trimethyl* 3 : 6-*anhydroglucose dimethylacetal* (X), from which the two methyl groups attached to position 1 can be removed by the agency of hot dilute sulphuric acid to give 2 : 4 : 5-*trimethyl* 3 : 6-*anhydro*aldehydo*glucose* (XI) (see Haworth, Jackson, and Smith, *loc. cit.*).

The furanoside structure of (II) and (III) was demonstrated by a comparison with methylated derivatives of 3 : 6-anhydroglucofuranose prepared for this purpose from 1 : 2-monoacetone 3 : 6-anhydroglucofuranose (XIII). This substance is known to have a furanose structure because it is derived from 1 : 2-monoacetone glucofuranose by a process which leaves the acetone residue intact (Ohle, von Vargha, and Erlbach, *Ber.*, 1928, **61**, 1214). Methylation of (XIII) with Purdie's reagents gives 1 : 2-*monoacetone*

5-*methyl* 3 : 6-*anhydroglucofuranose* (XIV) (isolated as a crystalline *hydrate*), from which the acetone residue is eliminated by heating with dilute sulphuric acid, yielding 5-*methyl*



3 : 6-*anhydroglucose* (XV). Oxidation of the latter with nitric acid furnishes 5-*methyl* 3 : 6-*anhydro-γ-gluconolactone* (XVI), which behaves as a typical γ-lactone in that it shows relatively slow mutarotation in aqueous solution; the lactone (XVI) is readily characterised by its conversion into the crystalline *amide* (XVII), in which the presence of a free hydroxyl group at C_2 is proved by the fact that it gives a positive Weerman test for α-hydroxy-amides. Treatment of 5-methyl 3 : 6-anhydroglucose (XV) or 5-methyl 1 : 2-monoacetone 3 : 6-anhydroglucofuranose (XIV) with acid methyl alcohol affords 5-*methyl* 3 : 6-*anhydro-methylglucoside*, which can only exist as the furanoside (XVIII) because the hydroxyl group in position 5 which would be involved in a pyranose structure is occupied by a methyl group. Further methylation of (XVIII) with Purdie's reagents gives 2 : 5-*dimethyl* 3 : 6-*anhydromethylglucofuranoside* (XIX), from which 2 : 5-*dimethyl* 3 : 6-*anhydroglucose* (XX) is prepared by hydrolysis with sulphuric acid. Although (XX) reduces Fehling's solution, it does not restore the colour to Schiff's reagent and in this respect it differs from the 2 : 4-dimethyl 3 : 6-anhydro*aldehydo*glucose (VII), previously mentioned, which reduces Fehling's solution and readily restores the colour to Schiff's reagent. The 2 : 5-dimethyl 3 : 6-anhydroglucose (XX) is easily recognised (*a*) by its conversion into a crystalline *anilide* and (*b*) by its oxidation with bromine to 2 : 5-*dimethyl* 3 : 6-*anhydro-γ-gluconolactone* (XXI) and conversion of the latter into the crystalline *amide* (XXII) of 2 : 5-dimethyl 3 : 6-anhydrogluconic acid. Like the 5-methyl 3 : 6-anhydro-γ-gluconolactone (XVI), the 2 : 5-dimethyl derivative (XXI) displays the typical slow mutarotation in aqueous solution characteristic of the γ-series of lactones.

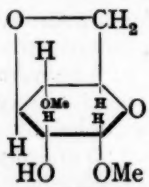
The structure of the 3 : 6-anhydromethylglucosides (II) and (III) was then determined as follows. Methylation of (II) and (III) with Purdie's reagents yields the corresponding *dimethyl* 3 : 6-*anhydromethylglucosides* (XXIII) and (XXIV), each of which undergoes hydrolysis on heating with 0·1N-sulphuric acid to give a dimethyl 3 : 6-anhydroglucose (XX). The anilide of the latter was identical with that of the authentic 2 : 5-di-

methyl 3 : 6-anhydroglucose prepared from monoacetone glucofuranose as previously described. The furanose structure of the methylglucosides (XXIII) and (XXIV), and therefore of (II) and (III), was further confirmed by converting the 2 : 5-dimethyl 3 : 6-anhydroglucose, obtained from (XXIII) and from (XXIV), successively into 2 : 5-dimethyl 3 : 6-anhydro-γ-gluconolactone (XXI) and the crystalline amide (XXII); these compounds were identical in every respect with the specimens obtained from 3 : 6-anhydroglucofuranose 1 : 2-monoacetone (XIII).

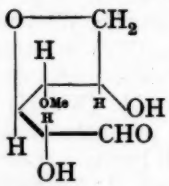
When 3 : 6-anhydro-α-methylglucopyranoside (I) is dissolved in 1% methyl-alcoholic hydrogen chloride, the extremely rapid formation of the anhydro-α-methylglucofuranoside (II) is accompanied by an instantaneous increase in the specific rotation from + 60° to + 145°; subsequently the rotation slowly falls to a constant value (+ 48°) simultaneously with the formation of an equilibrium mixture of the α- and the β-form of 3 : 6-anhydromethylglucofuranoside and no further change takes place when the solution is boiled. The same mixture of the α- and β-forms of anhydromethylglucofuranosides is produced when crystalline 3 : 6-anhydroglucose is treated with methyl-alcoholic hydrogen chloride either at room temperature or at the boiling point; both the α- and the β-form of 3 : 6-anhydromethylglucofuranosides (II) and (III) can be isolated from this equilibrium mixture by fractional crystallisation. Neither the α- nor the β-form of 3 : 6-anhydromethylglucopyranoside appears to be produced in this reaction, for complete methylation of the equilibrium mixture prepared either from 3 : 6-anhydro-α-methylglucopyranoside or from 3 : 6-anhydroglucose yields only 2 : 5-dimethyl 3 : 6-anhydro-αβ-methylglucofuranoside (XIX). The remarkable stability of the 3 : 6-anhydro ring in these substances is indicated by the fact that the direct oxidation of 5-methyl 3 : 6-anhydroglucose (XV) and 2 : 5-dimethyl 3 : 6-anhydroglucose (XX) with nitric acid affords an excellent method for the preparation of the corresponding lactones (XVI) and (XXI) respectively.

The facile conversion of the α- and β-forms of 3 : 6-anhydromethylglucopyranoside into the corresponding α- and β-methylfuranosides by the agency of a solution of mineral acid in organic solvents, referred to above, explains why the 2 : 5-dimethyl 3 : 6-anhydroglucose anilide and the 2 : 5-dimethyl 3 : 6-anhydrogluconamide (XXII) have been previously described as derivatives of 2 : 4-dimethyl 3 : 6-anhydroglucose (Peat and Wiggins, J., 1938, 1088).

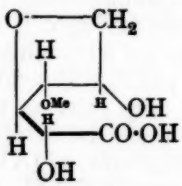
The location of the methyl group in the monomethyl 3 : 6-anhydro-α-methylglucopyranoside (XXV), obtained as an intermediate product in the preparation of 2 : 4-dimethyl



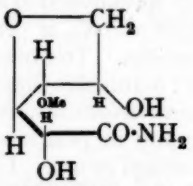
(XXV.)



(XXVI.)



(XXVII.)



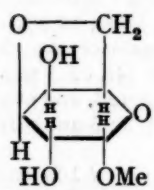
(XXVIII.)

3 : 6-anhydro-α-methylglucopyranoside (V), was ascertained as follows. Since complete methylation of (XXV) gives (V), the methyl group in (XXV) must occupy position 2 or 4. If the methyl group does not occupy position 4, then by analogy with 3 : 6-anhydro-α-methylglucopyranoside (I), it should be converted by means of dilute mineral acid into a monomethyl 3 : 6-anhydro-α-methylglucofuranoside. This monomethyl anhydro-α-methylglucoside (XXV), however, does not give a furanoside, but, like 2 : 4-dimethyl 3 : 6-anhydro-α-methylglucopyranoside (V), it undergoes hydrolysis when treated with 0·1N-sulphuric acid at room temperature to give a ***monomethyl 3 : 6-anhydroglucose***, a substance which shows aldehydic properties and probably possesses the structure shown in (XXVI). Moreover, if a free hydroxy-group occupies position 4, then (XXV), upon treatment with methyl-alcoholic hydrogen chloride, would be expected to behave like 3 : 6-anhydro-α-methylglucopyranoside and undergo the pyranoside ⟶ furanoside change, a transformation which proceeds rapidly and one which is accompanied by a considerable change in rotation. A solution of (XXV) in 1% methyl-alcoholic hydrogen chloride, however,

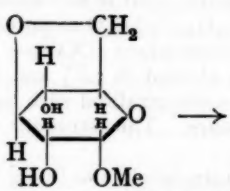
exhibits no mutarotation. Such evidence suggests that the methyl group occupies position 4. Further evidence that the methyl group is in position 4 is forthcoming from the fact that (XXVI) can be converted by means of bromine into the *monomethyl* 3 : 6-*anhydrogluconic acid* (XXVII), which, when treated with ethereal diazomethane, affords the corresponding *methyl* ester, a substance which can be distilled without showing any tendency to form a lactone. Treatment of the methyl ester with methyl-alcoholic ammonia yields the *amide* (XXVIII) of the 3 : 6-anhydromonomethylgluconic acid which shows a positive test for α-hydroxy-amides; it is clear, therefore, that in (XXVIII) the hydroxyl group is present in position 2 and therefore the methyl group of (XXV) must occupy position 4.

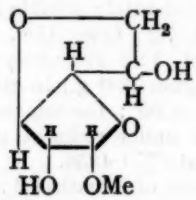
Discussion.

An examination of the model of 3 : 6-anhydroglucose shows that the adjacent hydroxyl groups on C_4 and C_5 are so situated as to allow of the formation of either a furanose or a pyranose ring; the models also make it clear, however, that the dicyclic system composed of the 3 : 6-anhydro ring and the 1 : 5-pyranose ring is under considerable strain, whereas the system containing the 3 : 6-anhydro ring and the 1 : 4-furanose ring is much less strained. This suggests an explanation of the observations that the α- and β-methylglucopyranosides readily change into the corresponding α- and β-methylfuranosides, for in so doing the molecule passes from a strained into a much less strained structural form. Probably for similar stereochemical reasons, the 3 : 6-anhydroglucose gives, when treated with acid methyl alcohol, 3 : 6-anhydro-α- and -β-methylglucofuranosides and not the glucopyranosides. In the galactose series (compare J., 1940, 1620), neither the α-form nor the β-form of 3 : 6-anhydromethylgalactopyranoside can be transformed into a furanoside because of the pronounced strain which would be introduced into the molecule. The models of the 3 : 6-anhydro-α- and -β-methylgalactopyranoside show clearly that this is due to the fact that the hydroxyl group at C_4, which would be involved in a galactofuranose structure, is in the reverse position from that of the hydroxyl group at C_4 in the 3 : 6-anhydroglucose series in which the pyranoside furanoside transformation takes place so readily (see below).



Galactose Series.





Glucose Series.

Noteworthy in this connection is the fact that 3 : 6-anhydrogluconolactone, which theoretically might possess either a 1 : 4- or a 1 : 5-lactone ring, was found to have the 1 : 4-γ-lactone structure; furthermore, both 2 : 5-dimethyl and 5-monomethyl 3 : 6-anhydro-γ-gluconolactone, which are comparatively strainless, are relatively quite stable in aqueous solution and behave as typical γ-lactones. The steric effect of the 3 : 6-anhydro ring, and the pronounced increase in strain which results from the introduction of the 1 : 5-pyranose ring, also explain the opening of the latter ring when 2 : 4-dimethyl 3 : 6-anhydromethylglucopyranoside is converted by means of an excess of methyl-alcoholic hydrogen chloride into the 2 : 4-dimethyl 3 : 6-anhydroglucose dimethylacetal. This steric effect of the 3 : 6-anhydro ring also explains the stability of the 2 : 4-dimethyl 3 : 6-anhydrogluconic acid and the failure to convert it into a lactone and, moreover, the reason for the existence of 2 : 4-dimethyl 3 : 6-anhydroglucose and 4-monomethyl 3 : 6-anhydroglucose as open-chain aldehydes is also apparent. It will be seen that in all these substances the final structure attained is the one which involves the least strain. Crystalline 3 : 6-anhydroglucose itself may exist in the dicyclic furanose form, but, even in this configuration, the presence of strain seems to be indicated by the fact that the open-chain aldehyde form of 3 : 6-anhydroglucose can be detected in aqueous solution by the positive test with Schiff's reagent (see Fischer and Zach, *loc. cit.*). The restoration of the

colour to Schiff's reagent is not effected as rapidly by 3 : 6-anhydroglucose as by 2 : 4-dimethyl 3 : 6-anhydro*aldehydo*glucose, and for this reason it is believed that in aqueous solution only a small portion of the 3 : 6-anhydroglucose exists in the open-chain aldehyde form. The formation of the dicyclic structure present in the 3 : 6-anhydro-α- and -β-methylglucopyranosides is apparently only possible because the 1 : 5-pyranose ring is stabilised (as methylpyranoside) before the anhydro ring is introduced. Of interest in this connection is an example in the galactose series in which the pyranose ring can be introduced after the 3 : 6-anhydro ring. The substance referred to is 2 : 4-dimethyl 3 : 6-anhydrogalactonic acid; this undergoes lactonisation on distillation, giving 2 : 4-dimethyl 3 : 6-anhydro-δ-galactonolactone, which contains the strained dicyclic system (Haworth, Jackson, and Smith, *loc. cit.*).

The exceptional properties of sugar derivatives possessing a 3 : 6-anhydro ring compel the conclusion that in these substances the anhydro ring takes on the character of the principal ring structure, to which the ordinary pyranose or furanose ring is only subsidiary. The remarkable changes outlined in this and the earlier paper (3 : 6-anhydrogalactose series) constitute a new aspect of the stability of pyranose and furanose forms; but it must be emphasised that these novel observations have no counterpart in the behaviour of the pyranosides and furanosides containing no anhydro ring. Indeed, in the latter we have sought in vain for similar analogies in properties.

Experimental.

1 : 2-Monoacetone 5-Methyl 3 : 6-Anhydroglucofuranose (XIV).—1 : 2-Monoacetone 3 : 6-anhydroglucofuranose (2·1 g.) prepared by the method of Ohle, von Vargha, and Erlbach (*Ber.*, 1928, **61**, 1214) was subjected to two methylations with Purdie's reagents; the mobile syrup isolated by means of acetone was distilled, giving *1 : 2-monoacetone 5-methyl 3 : 6-anhydroglucofuranose* (2·2 g.), b. p. (bath temp.) 115°/0·03 mm., $n_D^{22°}$ 1·4595 (Found : OMe, 14·3. $C_{10}H_{16}O_5$ requires OMe, 14·35%). On exposure to the atmosphere the substance crystallised as a *hydrate* of *1 : 2-monoacetone 5-methyl 3 : 6-anhydroglucofuranose*, m. p. 43—44°, $[\alpha]_D^{18°}$ + 82° in ethyl alcohol (*c*, 0·8) (after recrystallisation from water). The crystals were readily soluble in organic solvents, moderately soluble in water, and non-reducing to boiling Fehling's solution (Found : C, 53·0; H, 7·2; OMe, 14·0. $C_{10}H_{16}O_5,\frac{1}{2}H_2O$ requires C, 53·3; H, 7·6; OMe, 13·8%).

5-Methyl 3 : 6-Anhydro-γ-gluconolactone (XVI).—A solution of monoacetone 5-methyl anhydroglucose (2·0 g.) in ethyl alcohol (5 c.c.) and 0·1N-sulphuric acid (45 c.c.) was heated for 5 hours at 90°; the solution was neutralised with barium carbonate, filtered, and evaporated to a syrup under reduced pressure. This strongly reducing 5-methyl 3 : 6-anhydroglucose (1·55 g.) had $n_D^{20°}$ 1·4850.

A solution of 5-methyl 3 : 6-anhydroglucose (0·4 g.) in nitric acid (20 c.c., *d* 1·2) was heated for 20 hours at 50°. The solution was then diluted with water and freed from nitric acid by distillation under diminished pressure, water, and finally methyl alcohol, being added to facilitate the process; when quite free from solvent, the syrupy acid product was distilled, giving *5-methyl 3 : 6-anhydro-γ-gluconolactone* as a colourless viscous syrup (0·3 g.), b. p. (bath temp.) 165—170°/0·02 mm.; $n_D^{20°}$ 1·4835; $[\alpha]_D^{18°}$ + 109° (initial value) in water (*c*, 1·1), + 107° (after 2 hours), + 99° (25 hours), + 85° (70 hours), + 78° (116 hours), + 74° (174 hours), + 71° (240 hours) (mutarotation still incomplete). The sodium salt showed $[\alpha]_D^{18°}$ + 28° in water (*c*, 0·6) (calculated as lactone) and after acidification with dilute sulphuric acid the solution had $[\alpha]_D^{18°}$ + 31° (initial value), + 40° (after 30 hours), + 47° (71 hours), + 58° (166 hours), + 60° (261 hours) [Found : OMe, 17·7; equiv., 171 (by titration). $C_7H_{10}O_5$ requires OMe, 17·8%; equiv., 174].

5-Methyl 3 : 6-Anhydrogluconamide (XVII).—Treatment of the syrupy 5-methyl 3 : 6-anhydrogluconolactone (0·1 g.) with methyl-alcoholic ammonia afforded a crystalline amide in almost quantitative yield. After recrystallisation from ethyl alcohol–acetone, the *amide* of *5-methyl 3 : 6-anhydrogluconic acid* had m. p. 136—137°; $[\alpha]_D^{20°}$ + 68° in water (*c*, 0·6). A Weerman test upon this amide (20 mg.), carried out according to directions previously used, was positive (see Smith, J., 1939, 755; Bell, *ibid.*, p. 1871) (Found : C, 44·3; H, 6·9; OMe, 15·7; N, 7·6. $C_7H_{13}O_5N$ requires C, 44·0; H, 6·9; OMe, 16·2; N, 7·3%).

5-Methyl 3 : 6-Anhydromethylglucofuranoside (XVIII).—A solution of 5-methyl 3 : 6-anhydroglucose (1·1 g.) in 2% methyl-alcoholic hydrogen chloride (40 c.c.) was boiled for 8 hours, cooled, neutralised with silver carbonate, filtered, and concentrated under reduced pressure

to give syrupy 5-methyl 3 : 6-anhydromethylglucofuranoside. The latter was also obtained by boiling a solution of the 1 : 2-monoacetone 5-methyl 3 : 6-anhydroglucofuranose (1·8 g.) in 2% methyl-alcoholic hydrogen chloride (30 c.c.) for 6 hours. Simultaneous removal of the acetone residue and glycoside formation took place and after 6 hours the solution was cooled, neutralised with silver carbonate, filtered, and evaporated to give *5-methyl* 3 : 6-*anhydromethylglucofuranoside*, identical with that prepared by the first method, $n_D^{20°}$ 1·4730 (Found : OMe, 31·5. $C_8H_{14}O_5$ requires OMe, 32·6%).

2 : 5-*Dimethyl* 3 : 6-*Anhydromethylglucofuranoside* (XIX).—5-Methyl 3 : 6-anhydromethylglucofuranoside (1·6 g.) was subjected to two Purdie methylations, and the product distilled, giving 2 : 5-*dimethyl* 3 : 6-*anhydromethylglucofuranoside* as a colourless mobile liquid (1·6 g.), b. p. (bath temp.) 90—95°/0·03 mm.; $n_D^{23°}$ 1·4540 (Found : OMe, 45·5. $C_9H_{16}O_5$ requires OMe, 45·6%).

2 : 5-*Dimethyl* 3 : 6-*Anhydroglucose* (XX).—A solution of 2 : 5-dimethyl 3 : 6-anhydromethylglucofuranoside (0·6 g.) in 0·1N-sulphuric acid (22 c.c.) was heated on the boiling water-bath for 1·2 hours; the rotation then changed from $[\alpha]_D$ + 72° (initial value) to + 104° (constant value). After neutralisation of the mineral acid with barium carbonate, followed by filtration and the removal of the solvent under diminished pressure, there was obtained 2 : 5-*dimethyl* 3 : 6-*anhydroglucose* as a colourless viscous liquid (0·55 g.), b. p. (bath temp.) 120°/0·04 mm., $n_D^{18°}$ 1·4760; $[\alpha]_D^{18°}$ + 110° (initial value in water; *c*, 0·5), changing in 60 hours to + 120° (Found : OMe, 32·7. $C_8H_{14}O_5$ requires OMe, 32·6%).

2 : 5-*Dimethyl* 3 : 6-*Anhydroglucose Anilide*.—A solution of the 2 : 5-dimethyl 3 : 6-anhydroglucose (0·1 g.) and aniline (0·05 g.) in ethyl alcohol (2 c.c.) was boiled for 2 hours; removal of the solvent gave a syrup which solidified on cooling and, after recrystallisation from ethyl alcohol–ether the 2 : 5-*dimethyl* 3 : 6-*anhydroglucose anilide* had m. p. 96°; $[\alpha]_D^{18°}$ + 143° (equilibrium value in ethyl alcohol; *c*, 0·8) (Found : C, 63·3; H, 7·6; OMe, 23·2; N, 5·35. $C_{14}H_{19}O_4N$ requires C, 63·4; H, 7·2; OMe, 23·4; N, 5·3%).

2 : 5-*Dimethyl* 3 : 6-*Anhydro-γ-gluconolactone* (XXI).—A solution of 2 : 5-dimethyl 3 : 6-anhydroglucose (0·4 g.) in water (20 c.c.) was treated with bromine (2 c.c.) for 3 days at 40°. The solution was freed from the excess of bromine by aeration, neutralised with silver oxide, filtered before and after treatment with hydrogen sulphide, and evaporated under reduced pressure to give 2 : 5-*dimethyl* 3 : 6-*anhydro-γ-gluconolactone* as a liquid, b. p. (bath temp.) 130—135°/0·02 mm., $n_D^{18°}$ 1·4678; $[\alpha]_D^{18°}$ + 96° (initial value in water; *c*, 1·0), + 76° (after 96 hours), + 74° (144 hours), + 73° (200 hours, constant value) [Found : OMe, 32·2; equiv., 184 (by titration). $C_8H_{12}O_5$ requires OMe, 33·0%; equiv., 188].

Treatment of the 2 : 5-dimethyl 3 : 6-anhydro-γ-gluconolactone with methyl-alcoholic ammonia yielded the *amide* of 2 : 5-*dimethyl* 3 : 6-*anhydrogluconic acid* (XXII), m. p. 92°; $[\alpha]_D^{19°}$ + 41° in water (*c*, 0·7) (after recrystallisation from acetone–ether) (Found : C, 46·7; H, 7·4; OMe, 29·7; N, 6·8. $C_8H_{15}O_5N$ requires C, 46·8; H, 7·4; OMe, 30·2; N, 6·8%).

3 : 6-*Anhydroglucose*.—A solution of monoacetone 3 : 6-anhydroglucofuranose (32·2 g.) in 0·1N-sulphuric acid was heated for 1 hour on the boiling water-bath and was then neutralised with barium carbonate, filtered, and evaporated to dryness under reduced pressure to give a syrup which quickly crystallised. The crystals were dissolved in hot ethyl alcohol–ethyl acetate (1 : 1) and to the solution sufficient light petroleum was added to give a faint turbidity; on cooling, 3 : 6-anhydroglucose separated, m. p. 122° (yield, 21·4 g.). The anhydroglucose reduced boiling Fehling's solution and restored the colour to Schiff's reagent (5%) in a few minutes (see Fischer and Zach, *loc. cit.*).

3 : 6-*Anhydro-γ-gluconolactone*.—Oxidation of anhydroglucose (1·0 g.) in water (10 c.c.) with bromine (2 c.c.) at room temperature for 6 days afforded 3 : 6-anhydro-γ-gluconolactone. The solution was freed from the excess of bromine by aeration and from hydrobromic acid by neutralisation with silver oxide. The solution was then filtered, treated with hydrogen sulphide, and, after removal of the silver sulphide, evaporated under reduced pressure to give the crystalline lactone, m. p. 116° (after recrystallisation from ethyl alcohol–ether).

When this crystalline lactone was treated with methyl-alcoholic ammonia in the usual manner, the amide of 3 : 6-anhydrogluconic acid was obtained, m. p. 160°; $[\alpha]_D^{19°}$ + 109° in water (*c*, 1·0) (after recrystallisation from methyl alcohol) (Found : C, 40·8; H, 6·3; N, 7·9. Calc. for $C_8H_{11}O_5N$: C, 40·7; H, 6·3; N, 7·9%) {Fischer and Zach, *loc. cit.*, record m. p. *ca.* 149° (decomp.) and $[\alpha]_D^{20°}$ + 78° in water, for this amide}.

Complete methylation of the 3 : 6-anhydro-γ-gluconolactone (0·5 g.) was effected by two treatments with Purdie's reagents; the product, isolated by means of acetone, was a colourless mobile liquid (0·55 g.), b. p. (bath temp.) 130—140°/0·01 mm., $n_D^{18°}$ 1·4595 (Found : OMe, 37·5.

Calc. for 2 : 5-dimethyl 3 : 6-anhydrogluconolactone : OMe, 33·0%. Calc. for methyl 2 : 4 : 5-trimethyl 3 : 6-anhydrogluconate : OMe, 53·0%). The low refractive index and the high methoxyl content suggested that opening of the lactone ring had taken place to some extent. When this lactone was treated with methyl-alcoholic ammonia, there was obtained, in good yield, the crystalline amide of 2 : 5-dimethyl 3 : 6-anhydrogluconic acid, m. p. and mixed m. p. 92° (after crystallisation from acetone–ether). The original 3 : 6-anhydrogluconolactone must therefore be a γ-lactone.

The Action of Methyl-alcoholic Hydrogen Chloride upon 3 : 6-*Anhydroglucose.*—(a) *The structure of the* 3 : 6-*anhydromethylglucofuranoside.* A solution of 3 : 6-anhydroglucose (2·0 g.) in 1% methyl-alcoholic hydrogen chloride (110 c.c.) showed at room temperature $[\alpha]_D$ + 47° (initial value), changing in 1 hour to + 56° (constant value); no further change in rotation took place when the solution was boiled for 3 hours. Neutralisation of the hydrogen chloride with silver carbonate, followed by removal of the solvent, gave a syrupy mixture of the α- and the β-form of 3 : 6-anhydromethylglucofuranoside.

After three Purdie methylations the anhydro-αβ-methylglucoside yielded 2 : 5-dimethyl 3 : 6-anhydromethylglucofuranoside (2·17 g.), b. p. (bath temp.) 95°/0·03 mm., $n_D^{22°}$ 1·4545 (Found : OMe, 45·0%). Hydrolysis of this dimethyl anhydromethylglucoside was completed by heating for 1 hour at 20° with 5% hydrochloric acid; the specific rotation then changed from + 76° to + 95°. Neutralisation of the hydrochloric acid with silver carbonate, followed by removal of the solvent under diminished pressure, gave 2 : 5-dimethyl anhydroglucose, which was converted directly into the corresponding 2 : 5-dimethyl 3 : 6-anhydro-γ-lactone (see above), b. p. (bath temp.) 115—120°/0·02 mm., $n_D^{19°}$ 1·4668 (Found : OMe, 33·5%). When this lactone was treated with methyl-alcoholic ammonia, there was obtained in good yield the amide of 2 : 5-dimethyl 3 : 6-anhydrogluconic acid, m. p. and mixed m. p. 92° (after crystallisation from acetone–ether); neither the amide nor the ammonium salt of 2 : 4-dimethyl 3 : 6-anhydrogluconic acid could be detected (see below) and hence the mixture of glycosides prepared from the 3 : 6-anhydroglucose with acid methyl alcohol must be methylfuranosides.

(b) *The isolation of crystalline* 3 : 6-*anhydro-α- and -β-methylglucofuranoside.* A solution of 3 : 6-anhydroglucose (1·0 g.) in 1% methyl-alcoholic hydrogen chloride was kept for 1 hour at room temperature. Neutralisation of the solution with silver carbonate, followed by removal of the solvent, yielded a syrup, which was distilled, giving 3 : 6-anhydro-αβ-methylglucofuranoside, b. p. (bath temp.) 140—150°/0·04 mm., $n_D^{18°}$ 1·4912, $[\alpha]_D^{18°}$ + 38° in water (*c*, 1·0). The product, which did not reduce boiling Fehling's solution, crystallised spontaneously on keeping. A 1% solution of this 3 : 6-anhydro-αβ-methylglucofuranoside in 0·1N-sulphuric acid had at room temperature $[\alpha]_D^{18°}$ + 38° (initial value), + 41° (after 10 days), + 44° (22 days), + 52° (104 days) (hydrolysis still incomplete). A solution of the crystalline distillate in a little ethyl alcohol was diluted with ether and treated with light petroleum to give a slight turbidity. On standing at room temperature, needle-shaped crystals of 3 : 6-anhydro-α-methylglucofuranoside separated, followed by 3 : 6-anhydro-β-methylglucofuranoside in prisms. The two forms were separated mechanically and crystallised separately from ethyl alcohol–ether–light petroleum. The 3 : 6-*anhydro-α-methylglucofuranoside* (II) (0·25 g.) had m. p. 70°, $[\alpha]_D^{20°}$ + 164° in water (*c*, 0·9). A solution (0·6%) of the α-form in 0·1N-sulphuric acid at room temperature changed in 40 days from $[\alpha]_D$ + 164° (initial value) to + 126° (Found : C, 48·1; H, 7·0; OMe, 18·2. $C_7H_{12}O_5$ requires C, 47·7; H, 6·9; OMe, 17·6%). The 3 : 6-anhydro-β-methylglucofuranoside (III) (0·38 g.) had m. p. 98°, $[\alpha]_D^{20°}$ — 54° in water (*c*, 1·1) (Found : C, 48·1; H, 7·0; OMe, 17·9%). This β-form, which has also been obtained by Ohle and Wilcke (*Ber.*, 1938, **71**, 2324), showed $[\alpha]_D^{18°}$ — 54° (initial value) in 0·1N-sulphuric acid (*c*, 1·0), — 30° (after 11 days), — 4° (45 days).

Proof of the Structure of the 3 : 6-*Anhydro-α-methylglucofuranoside.*—The crystalline anhydro-α-methylglucoside (0·2 g.) was subjected to two Purdie methylations and there was obtained crystalline 2 : 5-*dimethyl* 3 : 6-*anhydro-α-methylglucofuranoside* (XXIII) (0·21 g.), m. p. 45°, $[\alpha]_D^{18°}$ + 208° in water (*c*, 1·0) (after recrystallisation from ether–light petroleum). The crystals were readily soluble in water, methyl and ethyl alcohols, chloroform, acetone, ether, and slightly soluble in light petroleum (Found : C, 53·0; H, 7·8; OMe, 44·6. $C_9H_{16}O_5$ requires C, 52·9; H, 7·9; OMe, 45·6%).

A solution of the 2 : 5-dimethyl 3 : 6-anhydro-α-methylglucofuranoside (0·11 g.) in 0·1N-sulphuric acid (6 c.c.) was heated on the boiling water-bath; the hydrolysis was followed polarimetrically : $[\alpha]_D$ + 207° (initial value), + 160° (after 1 hour), + 130° (2¼ hours), + 117° (3¼ hours), + 112° (4½ hours, constant value). Neutralisation of the sulphuric acid with barium carbonate, followed by the removal of the solvent under reduced pressure, gave 2 : 5-

dimethyl 3 : 6-anhydroglucofuranose as a liquid (0·08 g.), b. p. (bath temp.) 120—130°/0·03 mm., $n_D^{19°}$ 1·4750. On treatment with ethyl-alcoholic aniline the distillate readily afforded 2 : 5-dimethyl 3 : 6-anhydroglucose anilide, m. p. and mixed m. p. 95° (after recrystallisation from ethyl alcohol–ether).

Proof of the Structure of the 3 : 6-*Anhydro*-β-*methylglucofuranoside.*—Methylation of the anhydro-β-methylglucofuranoside (0·33 g.) with Purdie's reagents (two treatments) yielded a syrup, which was distilled, giving 2 : 5-*dimethyl* 3 : 6-*anhydro*-β-*methylglucofuranoside* (XXIV) as a colourless liquid (0·32 g.), b. p. (bath temp.) 100°/0·04 mm., $n_D^{19°}$ 1·4570, $n_D^{19°}$ 1·4550, $[\alpha]_D^{18°}$ + 15° in water (*c*, 2·0) (Found : OMe, 44·8%).

When a solution of the 2 : 5-dimethyl 3 : 6-anhydro-β-methylglucofuranoside (0·2 g.) in 0·1N-sulphuric acid (11 c.c.) was heated on the boiling water-bath, it showed $[\alpha]_D$ + 15° (initial value), + 59° (after 1 hour), + 83° (2 hours), + 97° (3½ hours), + 103° (4½ hours), + 104° (5½ hours, constant value). The 2 : 5-dimethyl 3 : 6-anhydroglucose, isolated as previously described, was obtained as a colourless oil, b. p. (bath temp.) 120—130°/0·01 mm., $n_D^{19°}$ 1·4745 (Found : OMe, 32·8%). On treatment with ethyl-alcoholic aniline in the usual way it furnished, in good yield, the corresponding anilide of 2 : 5-dimethyl 3 : 6-anhydroglucose, m. p. and mixed m. p. 95° (after recrystallisation from ethyl alcohol–ether).

A solution (1%) of 2 : 5-dimethyl 3 : 6-anhydro-β-methylglucofuranoside in 0·1N-sulphuric acid showed at room temperature $[\alpha]_D$ + 16° (initial value); + 24° (after 14 days); + 36° (45 days, hydrolysis still incomplete).

Synthesis of 3 : 6-*Anhydro*-α-*methylglucopyranoside* (I).—A solution of α-methylglucopyranoside (53 g.), prepared by the method of Patterson and Robertson (J., 1929, 303), in dry pyridine (250 c.c.) was treated with trityl chloride (74 g.) for 16 hours at room temperature and for 2 hours at 40°. The solution was diluted with a little water and poured into ice-water. The pyridine was removed from the syrupy product, most of it by trituration with water and the rest by extraction of a chloroform solution of the product with dilute sulphuric acid; the chloroform solution was washed with sodium bicarbonate and then with water and finally dried over anhydrous magnesium sulphate. Removal of the solvent yielded 6-trityl α-methylglucopyranoside as a glass, which was acetylated by treatment with pyridine (300 c.c.) and acetic anhydride (180 c.c.) for 24 hours at room temperature. The solution was poured into ice-water and a solution of the product in chloroform was washed with water, dilute sulphuric acid, sodium bicarbonate solution, again with water, dried over anhydrous magnesium sulphate, filtered, and evaporated under reduced pressure to a syrup. The 6-trityl 2 : 3 : 4-triacetyl α-methylglucopyranoside crystallised on trituration with a little methyl alcohol and after recrystallisation from acetone–ether–light petroleum, it had m. p. 136° (yield, 90 g.).

Removal of the trityl residue from the 6-trityl triacetyl α-methylglucoside by means of hydrobromic acid in acetic acid solution (Helferich, Klein, and Schäfer, *Ber.*, 1926, **59**, 79) yielded 2 : 3 : 4-triacetyl α-methylglucoside, m. p. 110°, which gave, on treatment with *p*-toluenesulphonyl chloride, 6-tosyl 2 : 3 : 4-triacetyl α-methylglucopyranoside, m. p. 86°, $[\alpha]_D^{18°}$ + 126° in chloroform (*c*, 0·7) (see Helferich, Brederick, and Schneidmüller, *Annalen*, 1927, **458**, 113) (Found : C, 50·65; H, 5·3; OMe, 6·7; S, 6·5. Calc. for $C_{20}H_{26}O_{11}S$: C, 50·6; H, 5·5; OMe, 6·5; S, 6·7%).

To a solution of 6-tosyl triacetyl α-methylglucoside (21·8 g.) in dry methyl alcohol (500 c.c.), sodium (30 mg.) was added; this Zemplén deactylation proceeded smoothly when the solution was kept at room temperature for 12 hours; on removal of the solvent under diminished pressure there was obtained crystalline 6-tosyl α-methylglucopyranoside, m. p. 110—112°, which crystallised well from hot water as the hydrate, in plates, m. p. 56—58°; yield, 17 g. (cf. Helferich and Himmen, *Ber.*, 1928, **61**, 1825).

The 6-tosyl α-methylglucopyranoside (8 g.) in ethyl alcohol (50 c.c.) was treated with N-sodium hydroxide (25 c.c.) for 12 hours at room temperature and for 1 hour at 80°. The solution was neutralised with carbon dioxide and evaporated to dryness under diminished pressure. Extraction of the residue with boiling acetone gave a quantitative yield of 3 : 6-anhydro-α-methylglucopyranoside, m. p. 108°; $[\alpha]_D^{20°}$ + 56° in water (*c*, 1·0) after recrystallisation from ethyl acetate (Found : C, 47·85; H, 6·6; OMe, 17·6. Calc. for $C_7H_{12}O_5$: C, 47·7; H, 6·9; OMe, 17·6%). Helferich, Klein, and Schäfer (*loc. cit.*) record m. p. 89—95°, $[\alpha]_D$ + 40° in water.

Conversion of 3 : 6-*Anhydro*-α-*methylglucopyranoside* (I) *into* 3 : 6-*Anhydro*-α-*methylglucofuranoside* (II).—(a) *With* 0·1N-*sulphuric acid.* A solution of 3 : 6-anhydro-α-methylglucopyranoside (0·1 g.) in 0·1N-sulphuric acid (10 c.c.) had (at room temperature) $[\alpha]_{5461}$ + 74° (after 10 mins.), + 84° (15 mins.), + 115° (45 mins.), + 152° (105 mins.), + 160° (135 mins.),

+ 167° (240 mins.), + 169° and $[\alpha]_D$ + 145° (960 mins.). At this stage the solution ($[\alpha]_D$ + 145°) was neutralised with barium carbonate, filtered, and evaporated to dryness under reduced pressure to give a crystalline residue. Recrystallisation from ethyl alcohol–ether gave 3 : 6-anhydro-α-methylglucofuranoside (0·06 g.), m. p. and mixed m. p. 68°, $[\alpha]_D^{20°}$ + 164° in water (*c*, 1·5). The syrupy residue obtained from the mother-liquor was slightly reducing to boiling Fehling's solution.

(b) *With a solution of hydrogen chloride in a mixture of ether and chloroform.* A solution of the α-methylpyranoside (50 mg.) in chloroform (1 c.c.) was quickly mixed with ethereal hydrogen chloride (1 c.c. of 5N), immediately poured into a dish, and quickly evaporated under reduced pressure over soda lime in a desiccator. The crystalline residue thus obtained was triturated with ether and after recrystallisation from ethyl alcohol–ether the 3 : 6-anhydro-α-methylglucofuranoside was obtained in needles (35 mg.), m. p. and mixed m. p. 70°, $[\alpha]_D^{18°}$ + 164° in water (*c*, 0·6). The residues were slightly reducing to Fehling's solution.

(c) *With methyl-alcoholic hydrogen chloride.* A solution of the α-methylpyranoside (50 mg.) in dry methyl alcohol (1 c.c.) was treated with one drop of 4N-methyl-alcoholic hydrogen chloride, poured immediately into a dish, and evaporated under reduced pressure over soda lime in a desiccator. Trituration of the crystalline residue with ether, followed by recrystallisation from ethyl alcohol–ether, yielded 3 : 6-anhydro-α-methylglucofuranoside (25 mg.), m. p. and mixed m. p. 69°, $[\alpha]_D^{18°}$ + 166° in water (*c*, 1·0).

Prolonged Treatment of 3 : 6-*Anhydro-α-methylglucopyranoside with* 1% *Methyl-alcoholic Hydrogen Chloride.*—A solution of 3 : 6-anhydro-α-methylglucopyranoside (1 g.) in methyl alcohol (40 c.c.) had $[\alpha]_D^{17°}$ + 60°. 1·5N-Methyl-alcoholic hydrogen chloride (10 c.c.) was then added and the solution showed $[\alpha]_D^{19°}$ *ca.* + 144° (after 2 mins.); + 140° (11 mins.); + 137° (17 mins.); + 124° (47 mins.); + 98° (120 mins.); + 90° (150 mins.); + 79° (210 mins.); + 75° (240 mins.); + 62° (360 mins.); + 56° (480 mins.); + 52° (600 mins.); + 50° (720 mins.) (constant value). The solution showed little or no change when boiled for 2 hours and there was no change when it was kept for 12 hours at room temperature. Neutralisation of the solution with silver carbonate, followed by removal of the solvent, gave syrupy 3 : 6-anhydro-αβ-methylglucofuranoside, which was subjected to two Purdie methylations; in this way there was obtained 2 : 5-dimethyl 3 : 6-anhydro-αβ-methylglucofuranoside (XIX) (1·0 g.), b. p. (bath temp.) 95—100°/0·04 mm., $n_D^{21°}$ 1·4550, $[\alpha]_D^{18°}$ + 85° in water (*c*, 0·6) (Found: OMe, 44·8%).

When a solution of the 2 : 5-dimethyl 3 : 6-anhydro-αβ-methylglucofuranoside (0·7 g.) in 0·1N-sulphuric acid (30 c.c.) was heated on the boiling water-bath, it showed $[\alpha]_D$ + 81° (initial value); + 98° (1·3 hours); + 102° (2 hours); + 105° (3 hours); + 107° (4 hours); + 108° (6 hours) (constant value). The solution was neutralised with barium carbonate, filtered, and evaporated under diminished pressure to give 2 : 5-dimethyl 3 : 6-anhydroglucose (XX) as a liquid (0·5 g.), b. p. 120°/0·04 mm., $n_D^{19°}$ 1·4750; $[\alpha]_D^{18°}$ + 112° (initial value) in water (*c*, 0·5), changing in 60 hours to + 121° (Found: OMe, 32·4%). Treatment of this reducing methylated sugar with boiling ethyl-alcoholic aniline as previously described gave the corresponding anilide of 2 : 5-dimethyl 3 : 6-anhydroglucose, m. p. and mixed m. p. 96°; $[\alpha]_D^{17°}$ + 180° in ethyl alcohol (*c*, 0·8), changing to + 145° (40 mins., equilibrium value) (the initial rotation is recorded with reserve, since the ethyl alcohol was warmed to dissolve the anilide) (Found: C, 63·4; H, 7·4; OMe, 23·0; N, 5·3. Calc. for $C_{14}H_{19}O_4N$: C, 63·4; H, 7·2; OMe, 23·4; N, 5·3%).

A solution of 2 : 5-dimethyl 3 : 6-anhydroglucose (0·3 g.) in nitric acid (5 c.c., *d* 1·42) was heated for 1 hour at 70° and for 4 hours at 85° in an open flask; the residual liquid was diluted with water and freed from solvent by evaporation under reduced pressure; the last traces of nitric acid were eliminated by simultaneous addition and distillation of methyl alcohol. Distillation of the syrupy acidic residue in the presence of a few mg. of barium carbonate gave 2 : 5-dimethyl 3 : 6-anhydro-γ-gluconolactone (XXI) (0·23 g.), b. p. (bath temp.) 130—140°/0·03 mm., $n_D^{17°}$ 1·4670 (Found: OMe, 32·0%). The colourless distillate reacted acid to Congo-paper, and showed $[\alpha]_D^{18°}$ + 100° (initial value) in water (*c*, 0·9); + 93° (11 hours); + 79° (100 hours); + 77° (175 hours); + 75° (24 days). Treatment of the 2 : 5-dimethyl 3 : 6-anhydro-γ-gluconolactone with methyl-alcoholic ammonia afforded the corresponding amide (XXII) in good yield, m. p. and mixed m. p. 92°, $[\alpha]_D^{17°}$ + 46° in water (*c*, 1·7) (Found: C, 46·7; H, 7·4; OMe, 30·4; N, 6·8. Calc. for $C_6H_{13}O_5N$: C, 46·8; H, 7·4; OMe, 30·2; N, 6·8%).

Methylation of 3 : 6-*Anhydro-α-methylglucopyranoside.* 4-*Methyl* 3 : 6-*Anhydro-α-methylglucopyranoside* (XXV).—3 : 6-Anhydro-α-methylglucopyranoside (0·55 g.), dissolved in acetone (5 c.c.), was methylated once with Purdie's reagents. Isolation of the product by means of

acetone afforded a crystalline substance, which gave 4-*methyl* 3 : 6-*anhydro*-α-*methylglucopyranoside* (0·2 g.), m. p. 152°, $[\alpha]_D^{17°}$ + 24° in water (*c*, 1·1) (after recrystallisation from acetone–ether) (Found : C, 50·3; H, 7·3; OMe, 32·7. $C_8H_{14}O_6$ requires C, 50·5; H, 7·45; OMe, 32·6%).

A solution (1·3%) of the 4-methyl 3 : 6-anhydro-α-methylglucopyranoside in 1% methyl-alcoholic hydrogen chloride showed $[\alpha]_D^{18°}$ + 25° (constant for 16 hours). A solution of 4-methyl 3 : 6-anhydro-α-methylglucoside (0·2 g.) in 0·1N-sulphuric acid (10 c.c.) had $[\alpha]_D^{18°}$ + 18° (after 10 mins.); − 5° (60 mins.); − 14° (120 mins.); − 16° (180 mins.) (constant value). The solution at this stage reduced Fehling's solution and restored the colour to Schiff's reagent; it was neutralised with lead carbonate, filtered, and evaporated under reduced pressure to give 4-*methyl* 3 : 6-*anhydroglucose* (XXVI) as a syrup (0·17 g.), $[\alpha]_D^{18°}$ − 17° in water (*c*, 0·7). This syrup also reduced Fehling's solution and gave a positive Schiff's test (Found : OMe, 16·5. $C_7H_{12}O_5$ requires OMe, 17·6%).

A solution of the 4-methyl 3 : 6-anhydroglucose (0·16 g.) in water (10 c.c.) was treated with bromine (0·5 c.c.) for 12 hours at room temperature in the presence of a slight excess of lead carbonate. After 12 hours, when the oxidation was completed, the solution was freed from the excess of bromine by aeration, filtered, and treated with hydrogen sulphide. Removal of the lead sulphide gave a colourless filtrate, which was concentrated to half volume under reduced pressure to remove hydrogen sulphide, neutralised with silver oxide, filtered before and after treatment with hydrogen sulphide, and evaporated to a syrup under diminished pressure. The 4-*methyl* 3 : 6-*anhydrogluconic acid* (XXVII) obtained in this way reacted acid to litmus and Congo-paper. This acid was dissolved in methyl alcohol and treated with an excess of an ethereal solution of diazomethane for approximately 5 minutes. Removal of the solvent yielded *methyl* 4-*methyl* 3 : 6-*anhydrogluconate* as a colourless liquid (0·13 g.), b. p. 125°/0·03 mm., $n_D^{19°}$ 1·4660, $[\alpha]_D^{19°}$ *ca.* + 2° in water (*c*, 2·4) (Found : OMe, 29·8. $C_8H_{14}O_6$ requires OMe, 30·1%).

The b. p. given here and in subsequent paragraphs is the bath temperature at which the substance distils.

Treatment of the methyl ester of 4-methyl 3 : 6-anhydrogluconic acid with methyl-alcoholic ammonia afforded the corresponding *amide* (XXVIII), which, however, failed to crystallise; it had $[\alpha]_D^{20°}$ − 7·5° in water (*c*, 2·1) and gave a positive Weerman test (carried out on 20 mg.) (Found : N, 7·5. $C_7H_{13}O_5N$ requires N, 7·3%).

2 : 4-*Dimethyl* 3 : 6-*Anhydro*-α-*methylglucopyranoside* (V).—A further methylation of the syrupy product obtained from the mother-liquor of 4-methyl 3 : 6-anhydro-α-methylglucopyranoside (see above) with Purdie's reagents gave 2 : 4-*dimethyl* 3 : 6-*anhydro*-α-*methylglucopyranoside* (0·2 g.), m. p. 66°, $[\alpha]_D^{16°}$ + 50° in water (*c*, 1·0) (Found : C, 53·2; H, 7·9; OMe, 45·2. $C_9H_{16}O_5$ requires C, 52·9; H, 7·8; OMe, 45·6%).

One methylation of the 4-methyl 3 : 6-anhydro-α-methylglucopyranoside (20 mg.) with Purdie's reagents also afforded 2 : 4-dimethyl 3 : 6-anhydro-α-methylglucopyranoside (18 mg.), m. p. and mixed m. p. 66°, $[\alpha]_D^{18°}$ + 49·5° in water (*c*, 1·6) (Found : OMe, 45·5%).

Transformation of 2 : 4-*Dimethyl* 3 : 6-*Anhydro*-α-*methylglucopyranoside* (V) *into the Corresponding* β-*Methylglucopyranoside* (VI).—Although not hygroscopic, the crystalline 2 : 4-dimethyl 3 : 6-anhydro-α-methylglucopyranoside is extremely sensitive to traces of acid; on exposure to the atmosphere of the laboratory it gradually changes to a non-reducing syrup having a negative rotation. By brief contact with air containing a trace of dry hydrogen chloride the α-form was immediately converted into a non-reducing syrup which had a negative rotation. The crystalline α-form (50 mg.) was dissolved in 5N-ethereal hydrogen chloride (1 c.c.) and immediately evaporated over soda lime in a vacuum desiccator; the syrup thus obtained did not reduce Fehling's solution, showed $[\alpha]_D^{18°}$ − 55° in water (*c*, 1·1), and therefore contained a considerable proportion of the 2 : 4-dimethyl 3 : 6-anhydro-β-methylglucopyranoside (see below).

A few crystals of the crystalline α-form were dried over phosphoric oxide and sealed in a dry glass tube; after 4 months the crystals had completely changed to a non-reducing syrupy mixture of the α- and the β-form of 2 : 4-dimethyl 3 : 6-anhydromethylglucopyranoside. The ease with which the α-form is converted into the β-form is illustrated by the fact that in one experiment methylation of 3 : 6-anhydro-α-methylglucopyranoside (2·0 g.) by three treatments with Purdie's reagents gave a syrupy product (1·6 g.), b. p. 100—110°/0·02 mm., $n_D^{22°}$ 1·4640, $[\alpha]_D^{18°}$ − 63° in water (*c*, 2·0) (Found : OMe, 45·4%). Evidently at some stage during the preparation partial transformation to the 2 : 4-dimethyl 3 : 6-anhydro-β-methylglucopyranoside had taken place.

Hydrolysis of 2 : 4-*Dimethyl* 3 : 6-*Anhydro*-α-*methylglucopyranoside*.—When a solution of

2 : 4-dimethyl 3 : 6-anhydro-α-methylglucoside (0·2 g.) in 0·1N-sulphuric acid was kept at room temperature, it showed $[\alpha]_D$ + 43° (after 0·1 hour); + 38° (0·2 hour); + 34° (0·3 hour); − 2° (1½ hours); − 15° (3 hours); − 20° (8 hours) (constant for a further 5 hours). Neutralisation of the solution with barium carbonate, followed by filtration and by the removal of the solvent under reduced pressure, gave 2 : 4-*dimethyl* 3 : 6-*anhydroglucose* (VII), which distilled as a colourless liquid (0·15 g.), b. p. 120—125°/0·03 mm., $n_D^{18°}$ 1·4750, $[\alpha]_D^{19°}$ − 28° in water (*c*, 1·7). This substance reduced Fehling's solution and gave a positive Schiff's test. It failed to give a crystalline anilide (Found : OMe, 32·2. $C_8H_{14}O_5$ requires OMe, 32·6%).

2 : 4-*Dimethyl* 3 : 6-*Anhydrogluconic Acid* (VIII).—A solution of 2 : 4-dimethyl 3 : 6-anhydroglucose (0·2 g.) in water (5 c.c.) was treated with bromine (0·5 c.c.) for 3 days at 40—45°. The solution was freed from the excess of bromine, neutralised with silver oxide, filtered before and after treatment with hydrogen sulphide, and evaporated to dryness under reduced pressure; 2 : 4-*dimethyl* 3 : 6-*anhydrogluconic acid* was obtained in this way, m. p. 156°; $[\alpha]_D^{20°}$ + 52° in water (*c*, 1·0), remaining unchanged after 3 days (after recrystallisation from acetone–ether–light petroleum). The acid showed an acid reaction to Congo-paper and could be titrated directly with sodium hydroxide. At 140°/0·04 mm. the 2 : 4-dimethyl 3 : 6-anhydrogluconic acid sublimed unchanged (Found : C, 46·6; H, 6·7; OMe, 30·4; equiv., 200. $C_8H_{14}O_6$ requires C, 46·6; H, 6·9; OMe, 30·1%; equiv., 206).

2 : 4-*Dimethyl* 3 : 6-*Anhydrogluconamide* (XII).—The 2 : 4-dimethyl 3 : 6-anhydrogluconic acid (25 mg.), dissolved in acetone, was esterified by treatment with a slight excess of ethereal diazomethane for about 5 minutes; removal of the solvent under reduced pressure gave the methyl ester as a colourless liquid. Treatment of this ester with methyl-alcoholic ammonia for 36 hours at 5° gave the *amide* of 2 : 4-dimethyl 3 : 6-anhydrogluconic acid, m. p. 155°, $[\alpha]_D^{19°}$ + 63° in water (*c*, 0·8) (Found : OMe, 30·1; N, 7·0. $C_8H_{15}O_5N$ requires OMe, 30·2; N, 6·8%).

Synthesis of 3 : 6-*Anhydro*-β-*methylglucopyranoside* (IV).—Well-powdered penta-acetyl glucose (15 g.) in a Carius tube was covered with liquid hydrogen bromide (*ca.* 25 c.c.) by passing the gas into the tube surrounded by liquid air. While the reaction mixture was still solid, the tube was sealed and left for 9 days at room temperature. The tube was cooled in liquid air until the reaction mixture was solid; it was then opened, and kept at room temperature until as much as possible of the hydrogen bromide boiled away from the light brown syrup, leaving a crystalline residue. A solution of this residue in chloroform (150 c.c.) was washed with water and sodium bicarbonate solution and finally dried over anhydrous magnesium sulphate. Removal of the solvent from the filtered solution gave acetodibromoglucose (6·5 g.), m. p. 170° (after recrystallisation from acetone–light petroleum) (see Fischer and Armstrong, *loc. cit.*).

The acetodibromoglucose (6·5 g.) was converted into 2 : 3 : 4-triacetyl β-methylglucopyranoside 6-bromohydrin by shaking with dry methyl alcohol in the presence of silver carbonate. The product had m. p. 124° (yield, 4·5 g.).

To a solution of the 2 : 3 : 4-triacetyl β-methylglucopyranoside 6-bromohydrin (4·9 g.) in dry methyl alcohol (50 c.c.), sodium (20 mg.) was added. After keeping overnight, the solution, on evaporation, gave β-methylglucopyranoside 6-bromohydrin (3·3 g.), m. p. 154° (after crystallisation from ethyl acetate). This bromohydrin (3·2 g.) was heated for 2 hours at 85—90° with N-sodium hydroxide (15 c.c.). After neutralisation with carbon dioxide, the solution was evaporated to dryness, and the residue exhaustively extracted with boiling acetone. Removal of the solvent gave a syrup, which distilled as a colourless liquid (1·64 g.), b. p. (bath temp.) 160—170°/0·02 mm., $n_D^{21°}$ 1·4900, $[\alpha]_D^{20°}$ − 138° in water (*c*, 1·1) (Found : OMe, 17·8. Calc. for $C_7H_{12}O_5$: OMe, 17·6%). This syrupy 3 : 6-anhydro-β-methylglucopyranoside (IV) crystallised, but owing to its hygroscopic nature a successful crystallisation was not obtained; the m. p. of the crude material was *ca.* 50° (sealed tube) (cf. Fischer and Zach, *loc. cit.*).

Transformation of 3 : 6-*Anhydro*-β-*methylglucopyranoside* (IV) *into* 3 : 6-*Anhydro*-β-*methylglucofuranoside* (III).—(a) *With a chloroform–ether solution of hydrogen chloride.* A solution of 3 : 6-anhydro-β-methylglucopyranoside (50 mg.) in chloroform (1 c.c.) was mixed with ethereal hydrogen chloride (1 c.c., 5N), poured quickly into a dish, and immediately evaporated over soda lime in a vacuum desiccator. Trituration of the crystalline residue with ether, followed by recrystallisation from ethyl alcohol–ether, gave 3 : 6-anhydro-β-methylglucofuranoside (35 mg.), m. p. and mixed m. p. 97°, $[\alpha]_D^{17°}$ − 50° in water (*c*, 1·1).

(b) *With methyl-alcoholic hydrogen chloride.* A 6% solution of the 3 : 6-anhydro-β-methylglucopyranoside in 1% methyl-alcoholic hydrogen chloride showed $[\alpha]_D^{18°}$ − 12° (after 0·2 hour); + 12° (0·7 hour); + 14° (1 hour); + 23° (3 hours); + 35° (7 hours); + 39° (10½ hours);

+ 48° (22½ hours); after the solution had been boiled for 1 minute, it showed (when cooled to room temperature) $[\alpha]_D$ + 56°. This final value is identical with that shown by an equilibrium mixture of the α- and the β-form of 3 : 6-anhydromethylglucofuranoside, prepared from the 3 : 6-anhydro-α-methylglucopyranoside and from 3 : 6-anhydroglucose (see above). It was clear, therefore, that in order to isolate the β-methylfuranoside (which has $[\alpha]_D$ − 50° in water), the reaction with acid methyl alcohol must be arrested quickly.

Accordingly, a solution of the 3 : 6-anhydro-β-methylglucopyranoside (45 mg.) in 1% methyl-alcoholic hydrogen chloride (2 c.c.) was kept for 4 minutes and then neutralised with silver carbonate. Removal of the solvent from the filtered solution gave a syrup, which crystallised on nucleation with the 3 : 6-anhydro-β-methylfuranoside; recrystallisation from ethyl alcohol–ether gave 3 : 6-anhydro-β-methylglucofuranoside (15 mg.), m. p. and mixed m. p. 97°, $[\alpha]_D^{21°}$ − 51° in water (*c*, 1·5).

The Action of 0·1N-*Sulphuric Acid upon* 3 : 6-*Anhydro*-β-*methylglucopyranoside.*—The substance underwent slow hydrolysis; a solution of 3 : 6-anhydro-β-methylglucopyranoside (0·11 g.) in 0·1N-sulphuric acid (11 c.c.) at room temperature had $[\alpha]_D$ − 136° (after 0·1 hour); − 123° (0·8 hour); − 100° (2 hours); − 86° (3 hours); − 22° (15 hours); − 20° (16 hours); − 18° (17 hours). The solution at this stage reduced Fehling's solution; it was neutralised with barium carbonate, filtered, and evaporated to dryness. Extraction of the residue with acetone at room temperature gave a syrup, which crystallised on nucleation with 3 : 6-anhydroglucose. Recrystallisation from ethyl acetate gave 3 : 6-anhydroglucose, m. p. and mixed m. p. 121°. No 3 : 6-anhydro-β-methylglucofuranoside could be isolated.

2 : 4-*Dimethyl* 3 : 6-*Anhydro*-β-*methylglucopyranoside* (VI).—3 : 6-Anhydro-β-methylglucopyranoside (0·5 g.), dissolved in acetone, was methylated three times with Purdie's reagents. The product, 2 : 4-*dimethyl* 3 : 6-*anhydro*-β-*methylglucopyranoside*, isolated by means of acetone, distilled as a colourless liquid (0·45 g.), b. p. (bath temp.) 85—90°/0·01 mm., $n_D^{22°}$ 1·4620, $[\alpha]_D^{18°}$ − 96° in water (*c*, 2·0) (Found: OMe, 46·0. $C_9H_{16}O_5$ requires OMe, 45·6%).

A solution of 2 : 4-dimethyl 3 : 6-anhydro-β-methylglucopyranoside (0·2 g.) in 0·1N-sulphuric acid showed (at room temperature) $[\alpha]_D$ − 96° (initial value); − 86° (2 hours); − 65° (15 hours); − 40° (39 hours); − 30° (63 hours); − 25° (92 hours); − 23° (112 hours); − 19° (160 hours) (constant value). The rate of hydrolysis was thus considerably slower than that of the 2 : 4-dimethyl 3 : 6-anhydro-α-methylglucopyranoside (see above). Neutralisation of the solution ($[\alpha]_D$ − 19°) with barium carbonate, followed by filtration and evaporation under reduced pressure, yielded 2 : 4-dimethyl 3 : 6-anhydroglucose (VII), which distilled as a colourless liquid (0·14 g.), b. p. (bath temp.) 115—120°/0·02 mm., $n_D^{18°}$ 1·4720 (Found: OMe, 32·5. Calc.: OMe, 32·6%).

The 2 : 4-dimethyl 3 : 6-anhydroglucose (0·12 g.), oxidised with bromine as previously described, gave 2 : 4-dimethyl 3 : 6-anhydrogluconic acid, m. p. and mixed m. p. 155° (after recrystallisation from ethyl alcohol–ether).

2 : 4 : 5-*Trimethyl* 3 : 6-*Anhydroglucose Dimethylacetal* (X).—A solution of 2 : 4-dimethyl 3 : 6-anhydro-αβ-methylglucopyranoside (0·52 g.) in 0·5% methyl-alcoholic hydrogen chloride (20 c.c.), when left at room temperature, showed $[\alpha]_D$ −14° (initial value); − 6° (0·1 hour); − 3° (0·2 hour); + 4° (0·7 hour); + 6° (1·5 hours); + 8° (3·5 hours) (constant for 15 hours). Neutralisation of the mineral acid with silver carbonate, followed by removal of the solvent, gave a syrup, which was then methylated once with Purdie's reagents; the product, isolated by means of acetone, was again treated with 0·5% methyl-alcoholic hydrogen chloride. Both treatments were repeated and after a further methylation with Purdie's reagents the product was distilled, giving 2 : 4 : 5-*trimethyl* 3 : 6-*anhydroglucose dimethylacetal* as a colourless mobile liquid (0·25 g.), b. p. (bath temp.) 110—120°/0·01 mm., $n_D^{18°}$ 1·4480, $[\alpha]_D^{18°}$ − 6° in water (*c*, 2·0) (Found: OMe, 57·2. $C_{11}H_{22}O_6$ requires OMe, 61·9%). This acetal formation does not proceed as well in the glucose series as in the corresponding compound of the galactose series and the presence of unchanged 2 : 4-dimethyl 3 : 6-anhydromethylglucoside may explain the low methoxyl content recorded above.

A solution of 2 : 4 : 5-trimethyl 3 : 6-anhydroglucose dimethylacetal (0·2 g.) in 0·1N-sulphuric acid at room temperature had $[\alpha]_D$ − 6° (initial value); − 12° (after 2 hours); − 14° (14 hours) (constant value); no change in rotation was observed when the solution was heated for 1 hour on the boiling water-bath. The solution was neutralised with barium carbonate, filtered, and evaporated to dryness under diminished pressure. Extraction of the residue with acetone gave a syrup, which on distillation afforded 2 : 4 : 5-*trimethyl* 3 : 6-*anhydro*aldehydo-*glucose* (XI) as a colourless mobile liquid (0·1 g.), b. p. (bath temp.) 105—110°/0·01 mm., $n_D^{18°}$ 1·4510. The distillate was strongly reducing to Fehling's solution and restored the colour

to Schiff's reagent almost immediately; 2 : 4 : 5-trimethyl 3 : 6-anhydro*aldehydo*glucose did not give a crystalline anilide (Found : OMe, 45·9. $C_9H_{16}O_5$ requires OMe, 45·6%).

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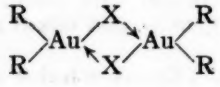
22. *The Organic Compounds of Gold. Part VIII. Dialkyl Gold Derivatives of Dibasic Acids.*

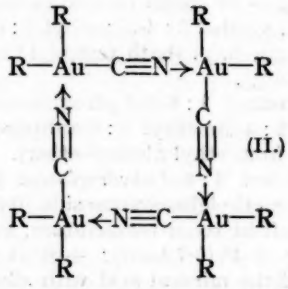
By CHARLES S. GIBSON and WILLIAM T. WELLER.

Tetraethylsulphatodigold contains four gold atoms in the molecule. It is soluble in water and in organic solvents. By interaction in aqueous solution with soluble salts of various acids other compounds are obtained and those with typical dibasic aliphatic and aromatic acids are described. The derivatives of oxalic and phthalic acids contain two gold atoms, those of higher members of the $C_nH_{2n}(CO_2H)_2$ (n = 1—6) series four gold atoms, and those of *iso*phthalic acid and the corresponding 4-nitro-compound six gold atoms in the respective molecules. Suggestions are made concerning the constitution of those compounds.

THE parent substances of the organic compounds of gold so far studied, although they are non-electrolytes, may be regarded as derivatives of the monobasic hydrochloric, hydrobromic, hydriodic and hydrocyanic acids (see Part VII, J., 1939, 762, for earlier references). These compounds are of two types, the molecular formulæ of which are planar and represented by (I) and (II), where R = alkyl and X = Cl, Br, I (J., 1937, 1690; *Proc. Roy. Soc.*, 1939, *A*, **173**, 147, 160).

(I.)





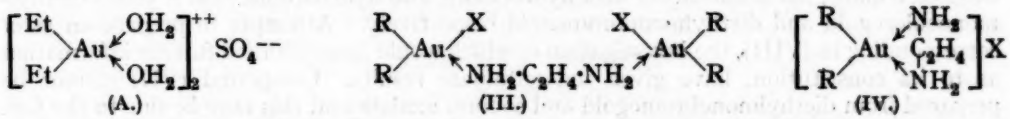
(II.)

In the course of other work (Gibson, E.P. 497,240) it was shown that, unlike related compounds, the product of interaction of silver sulphate is soluble not only in organic solvents, but also in water. By shaking " di-phenylethyl auric bromide " in benzene with an excess of silver sulphate, Kharasch and Isbell (*J. Amer. Chem. Soc.*, **1931**, **53**, 2701) obtained " di-phenylethyl auric sulphate," a colourless compound insoluble in water. They determined its gold content and showed that it could be sulphonated. They did not determine the molecular weight, but it was probably a sulphato-compound analogous to that now described.

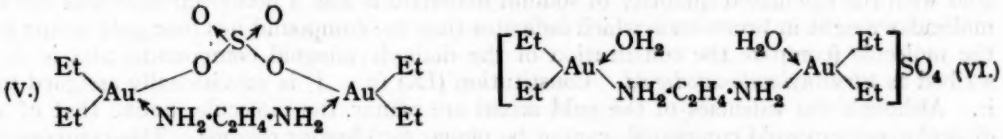
The colourless crystalline compound, readily prepared by shaking an excess of silver sulphate with an acetone solution of diethylmonobromogold, has the expected empirical formula, $(C_2H_5)_4Au_2SO_4$. Although it darkens somewhat rapidly on exposure to light, fresh preparations of the compound are easily manipulated. The compound is soluble in such solvents as acetone, alcohol, ethyl acetate and *cyclo*hexane and its molecular weight in boiling acetone indicates that the molecular formula is twice that of the empirical formula, so there are four gold atoms in the molecule. The substance may be described as *tetra-*

ethylsulphatodigold or more systematically as *bis(tetraethylsulphatodigold)* *; its constitution is discussed in the following paper. In aqueous solution the compound gives sulphate ions and has a molecular weight in agreement with the constitution (A), in which it is necessary to postulate the co-ordination of two molecules of water in order to preserve the 4-covalency of the auric gold atom. In aqueous solution the compound might be described as diethyldiaquoauric sulphate.

Unlike the dialkylhalogenogold compounds which yield ethylenediamine derivatives of two types—non-electrolytes of the general formula (III) † and electrolytes of the general formula (IV)—the above sulphato-compound yields only one compound with ethylenediamine. This is *ethylenediaminotetraethylsulphatodigold* (V), its molecule containing a



nine-membered heterocyclic ring. It is a colourless compound soluble in bromoform and in water. Since its aqueous solution contains sulphate ions, it is necessary to postulate that in aqueous solution the compound is ionised as indicated (VI).



2 : 2′-*Dipyridyltetraethylsulphatodigold* has a constitution similar to that of the ethylenediamino-compound and, like it, is soluble in water, giving sulphate ions. In this case, as with 2 : 2′-dipyridyltetraethyldibromodigold (Brain and Gibson, *loc. cit.*), the nitrogen atoms are attached to different gold atoms and attempts to prepare compounds in which both nitrogen atoms in dipyridyl are attached to the same gold atom have been unsuccessful.

Attempts to prepare tetramethylsulphatodigold have been unsuccessful and, although the tetra-*n*-butyl compound has been isolated, its instability made analysis and further investigation impossible. *Tetra*-n-*propylsulphatodigold* has been isolated and its properties are analogous to those of the tetraethyl compound. Its solubility in water appears to be lower than that of the tetraethyl compound and apparently higher than that of the tetra-*n*-butyl derivative. Aqueous solutions of the tetraethyl and the tetra-*n*-propyl compound may also be obtained by treatment of the ethylenediaminodialkylauric bromides with silver sulphate and, after separation of the silver halide, acidification of the filtrate with sufficient sulphuric acid to combine with the ethylenediamine.

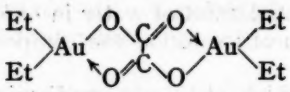
Aqueous solutions of the ethyl and the *n*-propyl compound react with aqueous solutions of salts of many acids, *e.g.*, hydrochloroplatinic, hydrochloroauric, acetic, phosphoric and tartaric acids, and also with sodium hydroxide, yielding precipitates; the compounds obtained with the sodium salts of representative dibasic organic acids have been studied in some detail. The colourless precipitates obtained by mixing aqueous solutions of the tetraethyl compound with hydrochloric, hydrobromic and hydriodic acids have been identified as diethylmonochlorogold, diethylmonobromogold, and diethylmonoiodogold respectively.

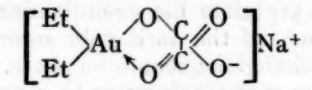
When aqueous solutions of equivalent quantities of tetraethylsulphatodigold and sodium oxalate are mixed, a colourless precipitate is obtained. This substance crystallises from ligroin in long colourless needles, and analysis and molecular weight determination (freezing *cyclo*hexane) confirm that it is *tetraethyloxalatodigold* (VII) (compare Mann and co-workers,

* In keeping with the nomenclature adopted in the work on organic compounds of gold, the substances are allotted names based on the simplest, frequently the empirical, formula and not necessarily on the molecular formula.

† Previous attempts to prepare *ethylenediaminotetraethyldibromodigold* (as III) have been unsuccessful (compare Brain and Gibson, J., 1939, 762); but this compound has now been obtained. It is colourless and insoluble in water. Like the methyl and *n*-propyl analogues, it decomposes with effervescence on melting.

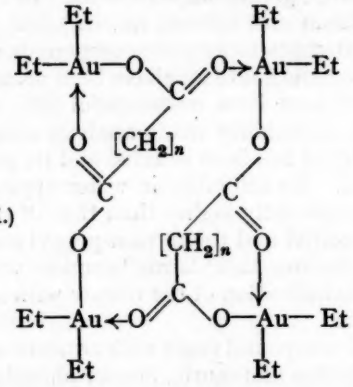
J., 1938, 2086). This compound is soluble in an aqueous solution of sodium oxalate and when an excess of the latter is used to react with tetraethylsulphatodigold, the precipitate first formed redissolves. The residue obtained by evaporation of the aqueous solution

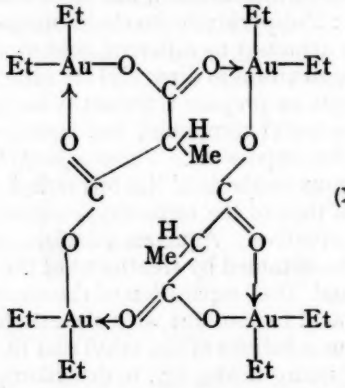
(VII.) 

 (VIII.)

to dryness at the ordinary temperature, on extraction with boiling ethyl alcohol, yields a sparingly soluble, crystalline compound, presumably the salt, *sodium diethyloxalatodigold* (VIII). The aqueous solution is very stable and undergoes little or no decomposition even on boiling; on acidification with hydrochloric and hydrobromic acid it yields diethylmonochlorogold and diethylmonobromogold respectively. Attempts to prepare an ester corresponding to (VIII), the investigation of which would have afforded further information as to its constitution, have given indeterminate results. Compound (VII) cannot be prepared from diethylmonobromogold and sodium oxalate and this may be due to the fact that, unlike the sulphato-compound, the bromo-compound has little, if any, tendency to become an electrolyte.

The colourless crystalline compound obtained by the interaction of tetraethylsulphatodigold with the calculated quantity of sodium malonate is also a non-electrolyte and has a molecular weight in bromoform which indicates that the compound has four gold atoms in the molecule (compare the constitution of the dialkylcyanogold compounds) and is described as *tetraethylmalonatodigold*. Constitution (IX) ($n = 1$) is provisionally assigned to it. Although the valencies of the gold atoms are planar, the molecule, unlike that of a dialkylmonocyanogold compound, cannot be planar for obvious reasons. This compound is not soluble in an aqueous solution of sodium malonate and it has not been possible to

(IX.) 

 (X.)

prepare a malonato-compound analogous to (VIII). Such a malonato-compound would have a ring system somewhat similar to that in the dialkylgoldacetylacetone compounds (J., 1930, 2531; 1939, 762) and the fact that derivatives analogous to (VIII) cannot be derived from compounds containing at least four gold atoms in the molecule may be connected with the stability of such heterocyclic systems, which apparently do not undergo a rearrangement similar to that which takes place when (VII) is converted into (VIII). It has not been possible to study the derivative of monomethylmalonic acid in any detail. The product obtained by mixing aqueous solutions of equivalent quantities of sodium monomethylmalonate and tetraethylsulphatodigold could not be recrystallised and its molecular weight was not determined. Analysis showed that the substance was *tetraethylmonomethylmalonatodigold* and, in all probability, its constitution is that indicated (X).

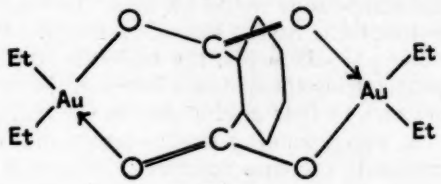
Analogous compounds of higher homologues of the normal acids of the $C_nH_{2n}(CO_2H)_2$ series ($n = 2$—6) have been investigated in the case of the *n*-propyl derivatives. As none of the five compounds is soluble in an aqueous solution of the sodium salt of the particular acid, excess of the latter could be employed in the preparation. The molecular weights of *tetra*-n-*propylsuccinatodigold*, *tetra*-n-*propylglutaratodigold*, *tetra*-n-*propyladipatodigold*,

tetra-n-*propylpimelatodigold* and *tetra*-n-*propylsuberatodigold* have been determined. In each case there are four gold atoms in the molecule, which may be represented conventionally by (IX) (Pr^n instead of Et, $n = 2$—6). No attempt is made at present to indicate the disposition of the $-[CH_2]_n-$ chains relative to the rest of the molecule. The last two compounds are particularly stable with definite melting points of the same order as those of pimelic and suberic acids themselves.

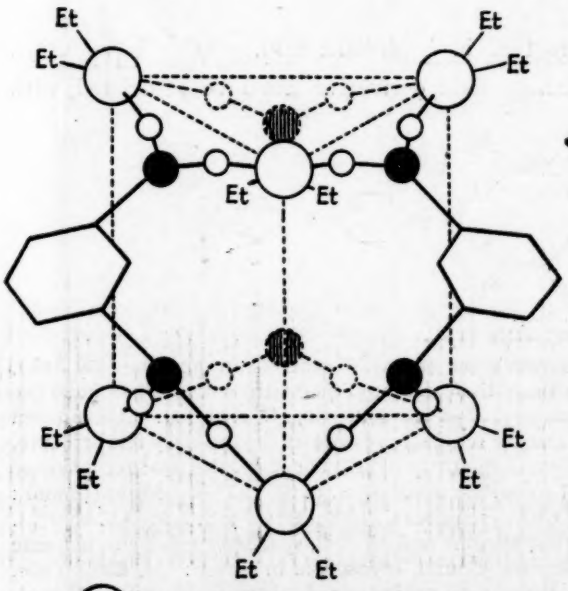
Tetraethylsaccharatodigold has been prepared; its solubility in water (about 0·2%) is surprisingly small. This compound proved to be too unstable in bromoform to permit a determination of its molecular weight.

Since attempts to isolate an azelato-derivative ($n = 7$) have been unsuccessful, it may be that the derivatives of acids higher in the series than suberic acid cannot be prepared.

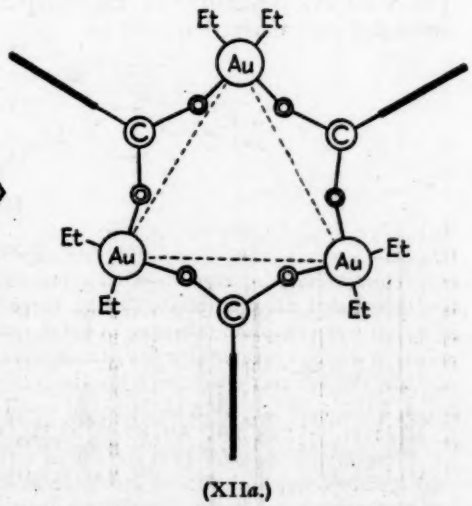
Representative derivatives of aromatic dicarboxylic acids have also been studied for comparison with those of the aliphatic acids. *Tetraethylphthalatodigold*, prepared from tetraethylsulphatodigold and an excess of sodium phthalate in aqueous solution, has a molecular weight in ethylene bromide indicating the presence of two gold atoms in the molecule and, to this extent, this compound is analogous to the oxalato-derivative (VII). It is, however, insoluble in an aqueous solution of sodium phthalate and is particularly stable. Its constitution is represented schematically by (XI); a rough calculation indicates that the $\begin{matrix}O\\O\end{matrix}\!>\!Au$ angle is probably not widely different from 90° and it is also



(XI.)



(XII.)



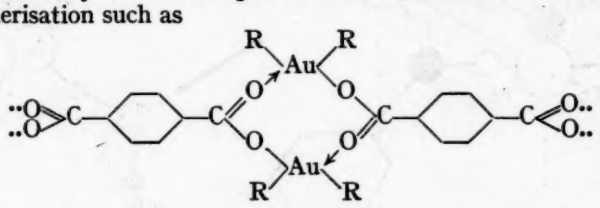
(XIIa.)

probable that the two gold atoms are in the same plane. *Tetraethyl-3-nitrophthalatodigold* proved to be too sparingly soluble for the determination of its molecular weight.

*Tetraethyliso**phthalatodigold*, prepared in the usual manner, is a colourless crystalline non-electrolyte insoluble in an aqueous solution of sodium *iso*phthalate; it is more soluble in organic solvents than the phthalato-compound. Its molecular weight in freezing *cyclo*hexane indicates that the molecule contains six gold atoms and this is also true of the molecule of *tetraethyl-4-nitroiso**phthalatodigold*. Substances containing six gold atoms in the molecule have not been previously described. Of various constitutions which can be suggested for such molecules, the most likely would appear to be one in which the gold atoms are at the corners of a regular triangular prism represented by (XII) and (XII*a*), each *iso*phthalato-group being placed as shown. In (XII) two of the *iso*phthalato-residues are shown in full and the carboxyl groups of the third (behind the back face of the prism) by broken circles. (XII*a*) is a projection of the same structure on the triangular base of the model.

To complete this series *tetraethylterephthalatodigold* has been prepared, but owing to its very low solubility no information regarding its molecular weight is available.

The co-ordinate link which each $\begin{matrix}R\\R\end{matrix}\!>$Au– group requires for stability in the compounds now described is not obtained by the formation of four-membered rings, $\begin{matrix}R\\R\end{matrix}\!>Au<\!\begin{matrix}O\\O\end{matrix}\!>$C–. Otherwise, it would be expected that each of the derivatives of the dicarboxylic acids would have a molecular weight indicating the presence of two gold atoms in the molecule and the three phthalic acid compounds would all have the same molecular weight. The co-ordinate link must therefore come from a second carboxyl. When the carboxyl groups are adjacent as in oxalic and phthalic acids, the molecule contains two gold atoms. In the case of the higher aliphatic acids the distance between the two carboxyl groups necessitates polymerisation from two to four gold atoms in the molecule. In the case of the *iso*phthalic acid (and of the corresponding 4-nitro-compound) derivative polymerisation to six gold atoms in the molecule becomes necessary. The polymerisation in this case is greater than in the case of the derivative of glutaric acid, which has, however, a carbon skeleton, $-O_2C\!<\!\begin{matrix}CH_2\\CH_2\end{matrix}\!>\!\begin{matrix}CH_2\\CO_2-\end{matrix}$, similar to that in *iso*phthalic acid, $-O_2C\!<\!\begin{matrix}C\\CH\end{matrix}\!>\!\begin{matrix}C\\CO_2-\end{matrix}$. The very low solubility of the terephthalic acid derivative could be associated with unlimited polymerisation such as



Experimental.

Tetraethylsulphatodigold.—Diethylmonobromogold (3 g.), dissolved in acetone (50 ml.), and powdered silver sulphate (3·5 g., three times the calculated quantity) were shaken until the reaction was complete (absence of bromo-compound in the solution; 4—5 hours). The filtered solution was evaporated in a dry atmosphere under reduced pressure at the ordinary temperature, and the residue recrystallised from the minimum quantity of ethyl acetate, the product (average yield, 2·0 g.; 73%) being obtained in small colourless needles, m. p. 96—97° (decomp.) (Found: C, 16·2; H, 3·7; S, 5·9; Au, 64·6. $C_8H_{20}O_4SAu_2$ requires C, 15·8; H, 3·3; S, 5·3; Au, 65·0%).

Tetraethylsulphatodigold is soluble in water, acetone and alcohol, sparingly soluble in benzene and *cyclo*hexane, and almost insoluble in ligroin [Found, cryoscopic in water: *M*, 230. Calc. for the compound fully dissociated into three ions as indicated above: *M*, 226. Found, ebullioscopic in acetone by the Landsberger–Walker method (*c*, 12·77, 12·7): *M*, 1235, 1360. Calc. for $C_{16}H_{40}O_8S_2Au_4$: *M*, 1212].

Ethylenediaminotetraethylsulphatodigold (V) was prepared by mixing an acetone solution of the sulphato-compound with an alcoholic solution of ethylenediamine (2 mols.). The colourless precipitate was washed with acetone. It may be recrystallised from ethyl alcohol (Found:

C, 18·35; H, 4·3; N, 4·4; S, 5·4; Au, 58·4. $C_{10}H_{28}O_4N_2SAu_2$ requires C, 18·0; H, 4·2; N, 4·2; S, 4·8; Au, 59·2%). The compound decomposes violently at about 147°. It is soluble in water and bromoform and almost insoluble in acetone and benzene.

The corresponding bromo-compound, *ethylenediaminotetraethyldibromodigold* (footnote, p. 103), was prepared by adding a ligroin solution of diethylmonobromogold (1 g.) to ethylenediaminodiethylgold bromide (1·18 g.) dissolved in methanol. The clear solution was evaporated under reduced pressure, and the residue extracted with light petroleum (b. p. 40—60°) to remove any unchanged diethylmonobromogold. The solid product was dissolved in purified acetone, and the filtered solution evaporated under reduced pressure in a dry atmosphere (Found: Br, 21·5; Au, 53·6. $C_{10}H_{28}N_2Br_2Au_2$ requires Br, 21·9; Au, 54·0%).

It was also prepared by mixing ethylenediamine (1 mol.) in ethyl alcohol with diethylmonobromogold (1 g.) in ligroin (15 ml., b. p. 60—80°). The colourless precipitate was washed with ligroin and dissolved in acetone, and the solution evaporated as described above (Found: Au, 53·2%).

The colourless compound is insoluble in water, sparingly soluble in ligroin and chloroform and soluble in alcohol and acetone. It decomposes with effervescence at about 113—114°.

2 : 2′-*Dipyridyltetraethylsulphatodigold* (as V) was prepared in good yield by mixing ethylalcoholic solutions of the sulphato-compound (0·5 g.) and 2 : 2′-dipyridyl (0·13 g.; 2 mols.) and evaporating the solution to dryness at the ordinary temperature. Excess of dipyridyl was removed by extraction with ligroin, the residue dissolved in the minimum quantity of ethyl alcohol, and acetone added to the filtered solution until, after cooling, colourless needles (0·4 g.), m. p. 162—163° (decomp.), separated (Found: C, 28·1; H, 3·6; N, 3·9; Au, 51·6. $C_{18}H_{28}O_4N_2SAu_2$ requires C, 28·3; H, 3·7; N, 3·7; Au, 51·7%).

The compound is soluble in water, alcohol and acetone; it is less soluble in *cyclo*hexane and apparently insoluble in ethyl acetate, ligroin and chloroform.

Tetra-n-propylsulphatodigold.—The solution obtained by shaking silver sulphate (16 g.) with di-*n*-propylmonobromogold (16 g.) in acetone (100 ml.) for 4½ hours was evaporated under reduced pressure over sulphuric acid at the ordinary temperature. The somewhat gummy residue, soluble in all the usual organic solvents, was extracted with warm light petroleum (b. p. 40—60°), and this filtered solution evaporated under reduced pressure in a desiccator. The residue was dissolved in a small quantity of methanol, and water added to the filtered solution until crystallisation began (Found: Au, 59·9. $C_{12}H_{28}O_4SAu_2$ requires Au, 59·5%).

This compound is less soluble in water and less stable than the ethyl compound; it is more soluble in organic solvents and can be recrystallised from *cyclo*hexane, in which, however, it is too sparingly soluble at the freezing point for molecular weight determination.

Following the usual procedure and taking advantage of its apparently low solubility in water and high solubility in organic solvents, attempts were made to isolate tetra-*n*-butylsulphatodigold, but the compound was not obtained in a form suitable for analysis. The attempted preparation of the tetramethyl compound starting with dimethylmonoiodogold was unsuccessful.

Tetraethyloxalatodigold (VII) was obtained as a colourless precipitate (0·43 g.) on mixing aqueous solutions of tetraethylsulphatodigold (0·5 g.) and of an equivalent quantity of sodium oxalate (0·113 g.). It was recrystallised from light petroleum (b. p. 40—60°) and obtained in long colourless needles, m. p. 81° (explosive decomp. at about 120°). The molecular weight was determined in freezing *cyclo*hexane (*c* 2·194) (Found: Au, 65·9; *M*, 568. $C_{10}H_{20}O_4Au_2$ requires Au, 65·9%; *M*, 598).

Tetraethyloxalatodigold is insoluble in water and soluble in the usual organic solvents. It undergoes decomposition even in the dark.

Sodium Diethyloxalatogold (VIII).—The sulphato-compound (0·7 g.) in water (10 ml.) was added to an aqueous solution of sodium oxalate (0·78 g.; 5 mols.) containing a little acetone to facilitate solution of (VII) which is first precipitated. The residue from evaporation of the clear solution to dryness at the ordinary temperature was extracted several times with boiling ethanol, and this solution filtered and evaporated (crude yield, 0·45 g.). The compound was recrystallised from ethanol and obtained in colourless soft needles (Found: Na, 6·0; Au, 53·4. $C_6H_{10}O_4NaAu$ requires Na, 6·3; Au, 53·9%).

The remaining compounds were all prepared by mixing aqueous solutions of the particular sulphato-compound and of the dibasic acid exactly neutralised with sodium (or potassium) hydroxide. Unlike (VII), these compounds are all insoluble in an excess of an aqueous solution of the salt of the dibasic acid, and an excess of the latter was used in many cases. When the compound could be crystallised, the solvent used is given in parentheses; otherwise, water-soluble substances were removed by thorough washing with water. The yields were practically

quantitative and all the substances are insoluble or, in the case of the saccharato-compound, only slightly soluble, in water.

Tetraethylmalonatodigold (as IX, $n = 1$) crystallises in colourless needles (acetone) which explode without melting at about 136°. It is soluble in bromoform and sparingly soluble in *cyclo*hexane [Found: C, 21·3; H, 3·5; Au, 64·4; *M* in freezing bromoform (*c* 1·197), 1150. $C_{22}H_{44}O_8Au_4$ requires C, 21·5; H, 3·5; Au, 64·3%; *M*, 1226].

Tetraethylmonomethylmalonatodigold (X) was obtained as a colourless precipitate and not recrystallised. Its melting was accompanied by decomposition (90—100°) and it decomposed explosively at about 140°. It was sparingly soluble in acetone and readily soluble in chloroform. Its molecular weight was not determined (Found: C, 23·3; H, 4·1; Au, 62·3. $C_{12}H_{24}O_4Au_2$ requires C, 23·0; H, 3·8; Au, 62·9%).

Tetra-n-*propylsuccinatodigold* (as IX, $n = 2$), obtained as a colourless precipitate, has m. p. 145—146° (decomp.). It is soluble in ligroin, *cyclo*hexane and benzene. It is unstable in bromoform [Found: C, 27·8; H, 4·4; Au, 57·6; *M* in freezing *cyclo*hexane (*c* 1·116) and benzene (*c* 3·955), 1387, 1280. $C_{32}H_{64}O_8Au_4$ requires C, 28·1; H, 4·7; Au, 57·8%; *M*, 1366].

Tetra-n-*propylglutaratodigold* (as IX, $n = 3$) crystallises in slightly discoloured needles (acetone). Its melting is accompanied by decomposition (about 90° onwards) [Found: C, 29·4; H, 4·9; Au, 56·2; *M* in freezing *cyclo*hexane (*c* 1·617), 1307. $C_{34}H_{68}O_8Au_4$ requires C, 29·3; H, 4·9; Au, 56·6%; *M*, 1394].

Tetra-n-*propyladipatodigold* (as IX, $n = 4$) crystallises in colourless needles (acetone), m. p. indef. (124—132°, decomp.). It is soluble in *cyclo*hexane and benzene [Found: C, 29·7; H, 4·7; Au, 55·4; *M* in freezing *cyclo*hexane and benzene, 1311 (*c* 1·621), 1243 (*c* 1·372), 1282 (*c* 3·769). $C_{36}H_{72}O_8Au_4$ requires C, 30·4; H, 5·1; Au, 55·5%; *M*, 1422].

Tetra-n-*propylpimelatodigold* (as IX, $n = 5$) crystallises in colourless soft needles (acetone), m. p. 79—81° (decomp. at about 100°) [Found: C, 32·1; H, 5·5; Au, 54·2; *M* in freezing *cyclo*hexane, 1295 (*c* 1·846). $C_{38}H_{76}O_8Au_4$ requires C, 31·5; H, 5·3; Au, 54·4%; *M*, 1450].

Tetra-n-*propylsuberatodigold* (as IX, $n = 6$) crystallises in colourless needles (acetone), m. p. 86—88° (decomp. from about 110°) [Found: C, 32·6; H, 5·4; Au, 53·4; *M* in freezing *cyclo*hexane, 1341 (*c* 1·546). $C_{40}H_{80}O_8Au_4$ requires C, 32·5; H, 5·5; Au, 53·4%; *M*, 1478].

Tetraethylsaccharatodigold crystallises in colourless needles (acetone–ethanol) and is not stable. It is sparingly soluble in *cyclo*hexane, readily soluble in chloroform and unstable in bromoform; its molecular weight could not be determined (Found: C, 23·4; H, 3·9; Au, 55·3. $C_{14}H_{22}O_8Au_2$ requires C, 23·4; H, 3·9; Au, 54·9%).

Tetraethylphthalatodigold (XI) was obtained as a colourless precipitate. It decomposes without melting from about 120° but at the ordinary temperature is very stable. It is sparingly soluble in the ordinary organic solvents, soluble in ethylene bromide and also in acetic acid, by which it is decomposed [Found: C, 28·9; H, 4·0; Au, 58·3; *M* in freezing ethylene bromide (*c* 0·4543, 0·4125), 577, 640. $C_{16}H_{24}O_4Au_2$ requires C, 28·5; H, 3·6; Au, 58·5%; *M*, 674].

Tetraethyl-3-nitrophthalatodigold, obtained as a colourless precipitate, was very sparingly soluble in organic solvents and its molecular weight could not be determined (Found: Au, 54·5. $C_{16}H_{23}O_6NAu_2$ requires Au, 54·9%).

Tetraethylisophthalatodigold (XII and XII*a*), obtained as a colourless precipitate, is sparingly soluble in acetone and ethanol and readily soluble in chloroform, bromoform and *cyclo*hexane. It crystallises in colourless needles (chloroform–acetone) and on heating decomposes without melting [Found: Au, 57·9; *M* in freezing *cyclo*hexane, 1793 (*c* 1·206), 1875 (*c* 2·228). $C_{48}H_{72}O_{12}Au_6$ requires Au, 58·5%; *M*, 2022].

Tetraethyl-4-nitroisophthalatodigold (as XII and XII*a*), obtained as a colourless precipitate sparingly soluble in the usual organic solvents, was sufficiently soluble in freezing *cyclo*hexane for molecular weight determination [Found: Au, 54·5; *M*, 2210 (*c* 0·9890). $C_{48}H_{69}O_{18}N_3Au_6$ requires Au, 54·9; *M*, 2187].

Tetraethylterephthalatodigold, obtained as a colourless precipitate, decomposes without melting and is very sparingly soluble in the usual organic solvents. Its molecular weight could not be determined (Found: Au, 58·4. $C_{16}H_{24}O_4Au_2$ requires Au, 58·5%).

The expenses of this investigation have been met by grants from Imperial Chemical Industries Ltd., to whom one of us (W. T. W.) is also indebted for a maintenance grant. We are grateful for assistance given by Drs. R. V. G. Ewens and F. H. Brain.

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23. *The Organic Compounds of Gold. Part IX. The Structure of Tetraethylsulphatodigold,* $(Et_2Au)_4(SO_4)_2$.

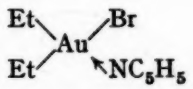
By Ronald V. G. Ewens and Charles S. Gibson.

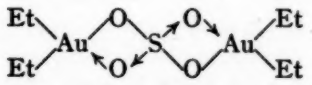
The most probable structure of the compound is deduced and discussed.

Pending a convenient opportunity for carrying out an *X*-ray investigation of this compound, apparently a polynuclear metallic complex of a novel type, it appears useful to record some considerations regarding its structure.

Any acceptable formula for this compound must incorporate three well-established principles: (i) In a purely covalent complex, each univalent Et_2Au group must be, to acquire stability, the acceptor of a further co-ordinate link, as for example in (I). The necessary co-ordinate links in the sulphato-compound can only be formed by the lone pairs of electrons of the oxygen atoms in the sulphate groups. (ii) The four valencies of each gold atom in the complex must lie in (or nearly in) a plane. (iii) The sulphate groups must be tetrahedral.

(I.)

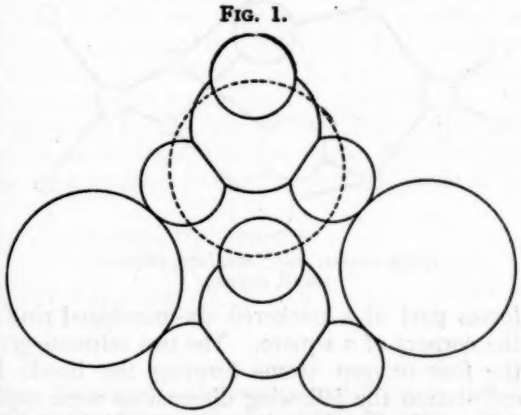




(II.)

Structure (II) would satisfy these conditions, but the observed molecular weight corresponding to double this formula (see preceding paper) renders this inadmissible. It must then be concluded that such a structure containing four-membered rings built up from one large (gold) atom and three smaller ones is unstable.* Calculation, using the observed radii of the atoms (see below), shows that the oxygen valency angle would be 90° and that of the gold atom would be reduced from the natural value of 90° to 70°. It would thus appear that no gold atom can be linked to two oxygen atoms in the same sulphate group.

Fig. 1.



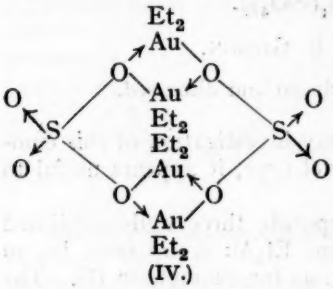
Large circles, gold; medium, sulphur; small, oxygen.

Now the four gold atoms in $(Et_2Au)_4(SO_4)_2$ require altogether the formation of four normal and four co-ordinate links with the oxygen atoms of the sulphate groups. Since these types of links differ only in the distribution of charge, they may, for the moment, be considered as equivalent. The following ways of distributing eight bonds between the eight oxygen atoms are then possible.

(*a*) If each oxygen atom forms only one link, it leads to the structure (III), represented in projection by Fig. 1, with the two sulphate groups in the same orientation, corresponding pairs of oxygen atoms being spanned only by a gold atom. The packing of the sulphate groups is very close. For a gold valency angle of 90° the angle between the oxygen–sulphur and oxygen–gold valency bonds is either 171° or 98°. Considerable distortion is therefore necessary for four of the oxygen valency angles. A more serious objection to this model is that some of the oxygen–oxygen and oxygen–sulphur separations between the two sulphate groups are only about 2·08 and 2·4 A. respectively. Both are thus 0·8 A. less than the sum of the so-called van der Waals radii (see Pauling, "Nature of the Chemical Bond," 1939, p. 176). Such a close approach of two unlinked atoms not themselves linked directly to a third has not been observed.

* Such four-membered rings have not yet been encountered and this point is also dealt with in the preceding paper.

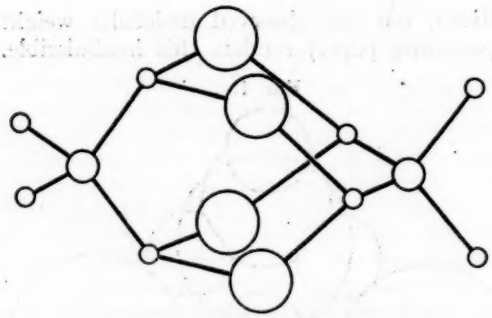
(*b*) It is therefore necessary to assume that four of the oxygem atoms take no part in bond formation with the gold atoms, each of the other four forming two bonds each.* This leads to structure (IV) or (V) (the latter shown in Figs. 2 and 3); the ethyl groups are omitted to make the diagrams clearer. In (IV) four-membered rings again feature, but, unlike those already mentioned, they involve two large gold atoms and are of a type well authenticated when halogen atoms are the bridging groups. The objection to this structure is not in the four-membered rings *per se* but in the resulting separation of the gold atoms in the separate rings, which would only be about 2·5 A. apart, 0·4 A. less than twice the covalent radius of gold.



(IV.)

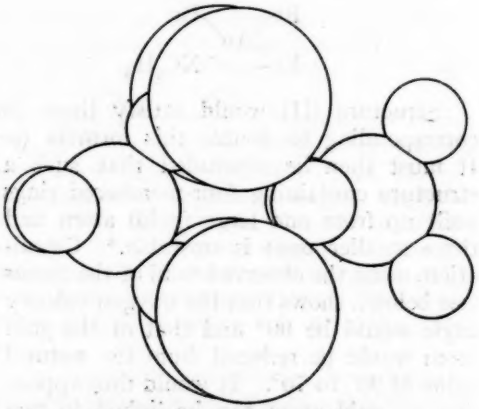
Structure (V) overcomes these difficulties. If the sulphur atom of one sulphate group is chosen as origin, the co-ordinates of the atoms are, from the symmetry of the model, as follows: S (0, 0, 0), (x, 0, 0); O (a, $\pm b$, 0), ($-a$, 0, $\pm b$), ($x+a$, $\pm b$, 0), ($x-a$, 0, $\pm b$); Au ($x/2$, $\pm c$, $\pm c$). Each gold atom

FIG. 2.



Large circles, gold; medium, sulphur; small, oxygen.

FIG. 3.



Large circles, gold; medium, sulphur; small, oxygen.

forms part of a puckered six-membered ring and the symmetry is such that they lie at the corners of a square. The two sulphate groups are similarly oriented in space, so that the four oxygen atoms forming the bonds lie at the corners of a tetrahedron. For calculation the following dimensions were used: Oxygen radius, 0·66 A.; sulphur radius, 1·04 A. (Pauling, *op. cit.*, p. 154); sulphate group tetrahedral with S–O bond 1·51 A. (*idem*, *ibid.*, p. 221); gold radius, 1·43 A.†

With these data it is possible to calculate all the other valency angles and interatomic distances in terms of one parameter x, the distance separating the two sulphur atoms. Parameters a and b are fixed by the dimensions of the sulphate group and c is a function of a, b, and x. The results are summarised:

x, A.	O–Au–O angle.	Au–O–Au angle.	S–O–Au angle.	Au–Au distance, A.
3·6	85° 30′	121° 28′	128° 8′	3·82
4·0	95° 52′	110° 28′	121° 5′	3·43
4·4	108° 37′	100° 16′	122° 2′	3·21
4·8	125° 00′	88° 1′	122° 6′	2·90
5·2	149° 45′	72° 18′	120° 4′	2·47

From these it appears that the most likely model is one in which the corresponding atoms of the two sulphate groups are separated by about 4 A. The natural gold valency angle

* Any distribution of valency bonds between the oxygen atoms which is less symmetrical than in (*a*) or (*b*) leads to most unlikely and unsymmetrical structures.

† Elliott and Pauling (*J. Amer. Chem. Soc.*, 1938, **60**, 1846) find Au–Cl in $AuCl_4$ to be 2·42 A. The radius of Cl being taken as 0·99 A., the radius of Au becomes 1·43 A.

of 90° is then increased only to about 96° and the oxygen valency angles differ little from the usual value. The adjacent gold atoms are then separated by about 3·4 A., *i.e.*, any pair of gold atoms linked to the same oxygen atom is separated by 0·5 A. more than twice the covalent radius of gold.

A model of this structure leads to a very rigid and close-packed assemblage in which the planar distribution of valencies around the gold atoms can be maintained.* The planes containing these sets of four valencies are, however, inclined to that of the square formed by the four gold atoms whose diagonals are rotational axes of symmetry, a rotation of 180° bringing the model into self-coincidence.

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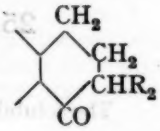
24. *Chalkones: Production of 2-Aryltetral-1-ones from Chalkone Dibromides via the Related β-Aroyl-α-arylpropionitriles.*

By M. SAMIULLA HIDAYETULLA, R. C. SHAH, and T. S. WHEELER.

A number of β-aroyl-α-arylpropionitriles have been prepared from the corresponding chalkone dibromides (see J., 1937, 1798) and converted by hydrolysis and subsequent reduction into the related αγ-diarylbutyric acids, some of which have been cyclised into 2-aryltetral-1-ones.

DODWADMATH and WHEELER (*Proc. Indian Acad. Sci.*, 1935, **2**, 438; see also Nadkarni *et al.*, J., 1937, 1798) observed that the action of warm alcoholic potassium cyanide on chalkone dibromides (II) gave β-aroyl-α-arylpropionitriles (III); this method of synthesis is sometimes more satisfactory than that of Hann and Lapworth (J., 1904, **85**, 1359), which involves the direct addition of hydrogen cyanide to the parent chalkone (I). A number of the nitriles (III) have now been prepared by the new method and hydrolysed to the corresponding propionic acids (IV), which have been reduced to the αγ-diarylbutyric acids (V). Some of the last compounds have been cyclised to the 2-aryltetral-1-ones (VI),

$$R_1{\cdot}CO{\cdot}CH{:}CHR_2 \longrightarrow \underset{\text{(I.)}}{R_1{\cdot}CO{\cdot}CHBr{\cdot}CHBrR_2} \longrightarrow \underset{\text{(II.)}}{R_1{\cdot}CO{\cdot}CH_2{\cdot}CHR_2{\cdot}CN} \longrightarrow \underset{\text{(III.)}}{R_1{\cdot}CO{\cdot}CH_2{\cdot}CHR_2{\cdot}CO_2H} \longrightarrow \underset{\text{(IV.)}}{R_1{\cdot}CH_2{\cdot}CH_2{\cdot}CHR_2{\cdot}CO_2H} \longrightarrow$$



(VI.)

(R_1 and R_2 = aryl)

of which few have hitherto been prepared (see Richardson, Robinson, and Seijo, J., 1937, 835; Newman, *J. Amer. Chem. Soc.*, 1938, **60**, 2947; Crawford, *ibid.*, 1939, **61**, 608). The conditions governing the cyclisation of a variety of γ-arylbutyric acids have been previously investigated (for references, see Attwood, Stevenson, and Thorpe, J., 1923, **123**, 1755: Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1939, **61**, 1272).

EXPERIMENTAL.

The required β-aroyl-α-arylpropionic acids were prepared from the corresponding chalkones *via* the dibromides and nitriles by the methods described by Nadkarni *et al.* (J., 1937, 1798). The following are new: β-*naphthyl* αβ-*dibromo*-β-p-*anisylethyl ketone*, m. p. (glacial acetic acid) 156° (Found: Br, 36·0. $C_{20}H_{16}O_2Br_2$ requires Br, 35·7%); β-(β-*naphthoyl*)-α-*phenylpropionitrile*, m. p. (alcohol) 128° (Found: N, 4·9. $C_{20}H_{15}ON$ requires N, 4·9%); β-(β-*naphthoyl*)-α-p-*anisylpropionitrile*, m. p. (alcohol) 121° (Found: N, 4·5. $C_{21}H_{17}O_2N$ requires N, 4·4%); β-p-*toluoyl*-α-p-*anisylpropionic acid*, m. p. (benzene) 151° (Found: C, 72·9; H, 6·1. $C_{18}H_{18}O_4$ requires C, 72·5; H, 6·0%); β-(β-*naphthoyl*)-α-*phenylpropionic acid*, m. p. (alcohol) 187° (Found: C, 78·8; H, 5·3. $C_{20}H_{16}O_3$ requires C, 78·9; H, 5·3%), and β-(β-*naphthoyl*)-

* The covalencies linking Au to the ethyl groups are known to be in the same plane as the other two valencies of the Au atom (J., 1937, 1690; *Proc. Roy. Soc.*, 1939, *A*, **173**, 147).

α-p-*anisylpropionic acid*, m. p. (alcohol–acetone) 173° (Found, C, 75·5; H, 5·8. $C_{11}H_{12}O$ requires C, 75·4; H, 5·4).

Reduction of Aroylarylpropionic Acids to the Corresponding Diarylbutyric Acids.—β-Benzoyl-α-*p*-anisylpropionic acid (10 g.) was refluxed with a mixture of toluene (200 c.c.), hydrochloric acid (1 : 1; 150 c.c.), and amalgamated zinc (100 g.) for 24 hours. A second equal portion of hydrochloric acid was added to the boiling reaction mixture after 12 hours. The liquid was filtered hot, and the solid residue washed with toluene. The combined lots of toluene were extracted several times with sodium carbonate solution, which was then acidified to separate α-p-*anisyl-γ-phenylbutyric acid* (1) (7 g.), m. p. (aqueous acetic acid) 98° (Found: C, 75·2; H, 6·7. $C_{17}H_{18}O_3$ requires C, 75·6; H, 6·7%). The following were similarly prepared in similar yield: α-*phenyl-γ*-p-*tolylbutyric acid* (2), m. p. (hexane) 80° (Found: C, 79·8; H, 7·2. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%); α-p-*anisyl-γ*-p-*tolylbutyric acid* (3), m. p. (dilute alcohol) 115° (Found: C, 76·1; H, 7·2. $C_{18}H_{20}O_3$ requires C, 76·1; H, 7·0%); α-3 : 4-*methylenedioxyphenyl-γ-phenylbutyric acid* (4), m. p. (hexane) 98° (Found: C, 72·2; H, 5·5. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·6%); α-3 : 4-*methylenedioxyphenyl-γ*-p-*tolylbutyric acid* (5), m. p. (dilute alcohol) 96° (Found: C, 72·6; H, 5·9. $C_{18}H_{18}O_4$ requires C, 72·5; H, 6·0%); and α-p-*anisyl-γ*-β-*naphthylbutyric acid*, m. p. (dilute alcohol) 132° (Found: C, 78·9; H, 6·6. $C_{21}H_{20}O_3$ requires C, 78·8; H, 6·3%).

Cyclisation of Diarylbutyric Acids to 2-Aryltetral-1-ones.—2-p-*Anisyltetral-1-one*, m. p. (dilute alcohol) 107° (Found: C, 80·7; H, 6·7. $C_{17}H_{16}O_2$ requires C, 81·0; H, 6·3%), separated as an oil (0·5 g.) which afterwards solidified from a solution of (1) (1 g.) in phosphoryl chloride (3 c.c.) which had been refluxed (calcium chloride guard) for 10 mins., cooled, and poured on ice. The *oxime*, which was formed by heating the ketone for 5 hours with hydroxylamine hydrochloride in pyridine solution, had m. p. (dilute alcohol) 126° (Found: N, 4·9. $C_{17}H_{17}O_2N$ requires N, 5·2%). 2-*Phenyl-7-methyltetral-1-one*, m. p. (aqueous alcohol) 67° (Found: C, 86·2; H, 7·2. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8%), and 2-p-*anisyl-7-methyltetral-1-one*, m. p. (aqueous alcohol) 108° (Found: C, 81·8; H, 6·7. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8%), were similarly prepared in similar yield from (2) and (3), respectively. Solidification of the oils which first separated was accelerated by alkali extraction of the chloroform solution. Attempts to cyclise (4) and (5) were unsuccessful.

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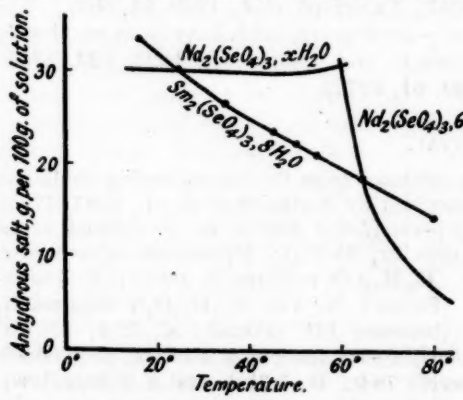
25. *Samarium Selenate and its Solubility in Water.*

By J. NEWTON FRIEND.

The solubility of the octahydrate in water has been determined between 16° and 80°.

THE selenates of lanthanum, praseodymium, and neodymium have already been studied (Friend, J., 1931, 1802; 1932, 1597, 2410) with a view to their use in the separation of the rare-earth elements by fractional crystallisation. Two hydrates of samarium selenate were described by Cleve (*Bull. Soc. chim.*, 1885, **43**, 162), *viz.*, the octahydrate, which crystallised from solution at room temperature, and the dodecahydrate, which separated below 10°. Cleve stated that the octahydrate was more soluble than the corresponding sulphate, with which it is isomorphous, but no systematic determination of its solubility appears to have been made.



EXPERIMENTAL.

The selenate used was prepared by dissolving the oxide in dilute selenic acid and crystallising it on the water-bath, the salt being much less soluble in hot water than in cold.

The octahydrate, $Sm_2(SeO_4)_3,8H_2O$, separates from aqueous solution at all temperatures

between about 10° and 100°, and is stable in dry air. The following analyses were made on specimens prepared as follows: (1) Concentration of an acidified solution over concentrated sulphuric acid at 18°; the crystals were crushed and dried between filter-paper. (2) An acidified solution was heated on the water-bath; the crystals separating were drained on a sintered-glass funnel and dried between filter-paper. (3) and (4) Crystals prepared as in (2) and dried over sulphuric acid for 4 days and several weeks respectively. (5) A neutral solution was taken to dryness in a platinum dish on a water-bath: partial dehydration appears to have occurred. (6) The decahydrate was exposed to air at 18° until constant in weight.

	1.	2.	3.	4.	5.	6.	Calc. for octahydrate.
Sm_2O_3, %	39·65	39·85	40·14	40·16	40·32	40·13	39·92
$3SeO_3$, %	43·13	43·54	43·86	43·73	44·05	44·80	43·59
H_2O (by diff.), % ...	17·22	16·61	16·00	16·11	15·63	16·07	16·49
Ratio Sm_2O_3 : 3Se ...	1·478	1·472	1·472	1·473	1·472	1·440	1·473

The solubility of the octahydrate in water was determined in the apparatus already described (Friend, J., 1930, 1633), a sintered-glass funnel of the finest grade, No. 4, being used. The samaria and selenium were estimated by methods analogous to those employed for the neodymium salt (Friend, J., 1931, 1802); they were found to give closely concordant results. It was necessary to work with slightly acidified solutions in order to prevent precipitation of basic salt, particularly at the higher temperatures. This rendered accurate reproducibility of the results extremely difficult.

The results were as follows, *S* giving the solubility as g. of anhydrous samarium selenate per 100 g. of solution:

Temp.	*S.*	Sm_2O_3 : Se.	Temp.	*S.*	Sm_2O_3 : Se.
16·6°	33·60 *	1·395	50·0°	22·15 *	1·327
17·0	34·30	1·488		22·07	1·281
25·0	31·01	1·468		21·93	1·260
	30·21 *	1·351	55·0	21·13 *	1·321
	28·31	1·274		19·35	1·022
35·2	27·52	1·456	64·6	20·38	1·613
	26·42 *	1·322		18·62 *	1·207
45·0	24·85	1·386	65·0	17·65	0·953
	23·56 *	1·276		16·46	0·905
	23·28	1·293	80	14·00 *	1·353
				14·03	1·263

The asterisked data are shown in the figure together with the results previously obtained with neodymium selenate. The curves show that fractional crystallisation of the selenates does not offer a good method of separating samarium from neodymium. Excess of selenic acid reduces the solubility of the salt.

THE TECHNICAL COLLEGE, BIRMINGHAM. [*Received, October 21st*, 1940.]

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26. *The Structure of the Nitroindazoles and their* N-*Methyl Derivatives.*

By IAN M. BARCLAY, NEIL CAMPBELL, and GEORGE DODDS.

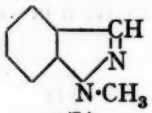
The bromine reactivity of the *N*-methyl derivatives of three 3-bromonitroindazoles has been measured, and the results discussed in relation to the structures of indazole and its derivatives. Evidence is given for the quinonoid formula for 2-alkylindazoles. There are indications that indazole resembles in structure the 1-alkyl compounds, and this is confirmed by absorption-spectra measurements.

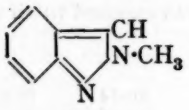
The validity of the Auwers rule for the alkylation of indazoles is questioned.

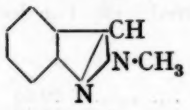
THE structure of indazole and its derivatives has been intensively studied by Auwers and others (see, *e.g.*, Auwers and Duesberg, *Ber.*, 1920, **53**, 1179; Auwers and Schwegler, *ibid.*, p. 1211; Auwers, *Annalen*, 1924, **437**, 70; Meisenheimer and Diedrich, *Ber.*, 1924, **57**, 1715; Fries, *Annalen*, 1927, **454**, 303) both by chemical and by physical methods. By analogy with other heterocyclic compounds there can be little doubt that indazole

and its derivatives are resonance hybrids, the resonance being largely due to that of the benzene nuclei (cf. Pauling and Sherman, *J. Chem. Physics*, 1933, **1**, 606), though the necessary data are lacking to test the matter quantitatively. The present paper deals mainly with the structure of the heterocyclic ring.

1-Methylindazole is represented without ambiguity by (I), but the structure of the 2-compound has not yet been settled. Auwers (*loc. cit.*, 1924) rejects (III) and accepts


(I.)

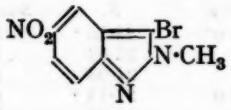

(II.)

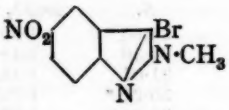

(III.)

(II), pointing out the difficulty of constructing a molecule with a three-membered ring. Meisenheimer (*loc. cit.*) supports this view, but Fries (*loc. cit.*) prefers (III), as the 2-alkylindazoles are colourless and show no quinonoid properties. Our results show that one of the forms contributing to the hybrid is the quinonoid structure.

It is known that, if a bromo-group is separated from a nitro-group by a double bond or conjugated system of double bonds, the bromine is reactive towards piperidine (*e.g.*, McLeish and Campbell, J., 1937, 1103) and this method of double-bond detection is applied in the present paper to derivatives of the nitroindazoles.

Consideration of the possible formulæ for the methyl derivatives of all the 3-bromo-*x*-nitroindazoles shows that reactive bromine will be found only in one compound, *viz.*,

(IV.) 


(V.)

3-bromo-5-nitro-2-methylindazole and then only if it possesses a quinonoid structure as one of the contributory forms (IV). That this is indeed the case is shown by the following table giving the removal of bromine by piperidine under different conditions.

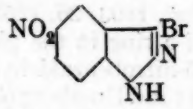
Compound.	Removal of bromine, %. i.	ii.	iii.
3-Bromo-4-nitroindazole		0	
3-*Bromo*-4-*nitro*-1-*methylindazole*	0	0	
3-Bromo-4-nitro-2-methylindazole	0	0	
3-*Bromo*-5-*nitroindazole*	0	4	0 1
3-*Bromo*-5-*nitromethylindazole*, m. p. 188°	2	30	44 45
3-*Bromo*-5-*nitromethylindazole*, m. p. 225°	0	0	0 0
3-Bromo-6-nitroindazole			0 2
3-*Bromo*-6-*nitro*-1-*methylindazole*	0	0	0 2
3-*Bromo*-6-*nitro*-2-*methylindazole*	0	0	0 0

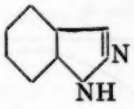
Col. i. Piperidine at 45° for 1 hour.
Col. ii. Piperidine at 45° for 24 hours.
Col. iii. Piperidine at 95° for 3 hours.

It therefore is necessary to assign an *o*-quinonoid structure to 3-bromo-5-nitro-2-methylindazole, and by analogy it is probable that all 2-alkylindazoles possess this structure. This conclusion is supported by Auwers's refractivity measurements (*Annalen*, 1937, **527**, 291). It might be argued that the three-membered ring formula (V) would account for the reactivity by the N_1–C_3 bond, but if this were so the 2-alkyl derivatives of all 3-bromoindazoles should show bromine reactivity. This is not the case.

The results of the bromination of the 5-nitromethylindazoles were as follows: methyl compound, m. p. 163° ⟶ bromo-compound, m. p. 225°; methyl compound, m. p. 129° ⟶ bromo-compound, m. p. 188°. As the bromo-compound, m. p. 188°, is reactive, it must be methylated in the 2-position, and hence its precursor, m. p. 129°, must also be the

2-derivative. Hence the isomer, m. p. 163°, is 5-nitro-1-methylindazole. This is the opposite of the formula assigned by Fries (*loc. cit.*), who, however, noted that his evidence was inconclusive.

(VI.) 



(VII.)

The small reactivity of 3-bromo-5-nitroindazole indicates that structure (VI) is the main contributing form, and suggests that the corresponding form (VII) holds for indazole. This is in agreement with Auwers's conclusion (previous reference) that indazole closely resembles the 1-alkyl derivatives, *e.g.*, (I). Further support for this conclusion is provided by the absorption spectra of indazole, 5- and 6-nitroindazoles, and their *N*-methyl-

FIG. 1.

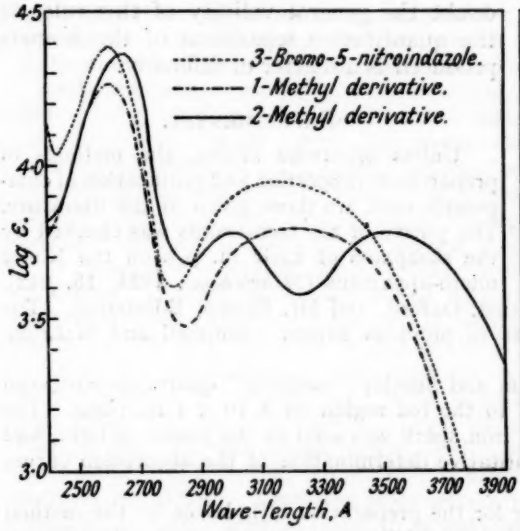
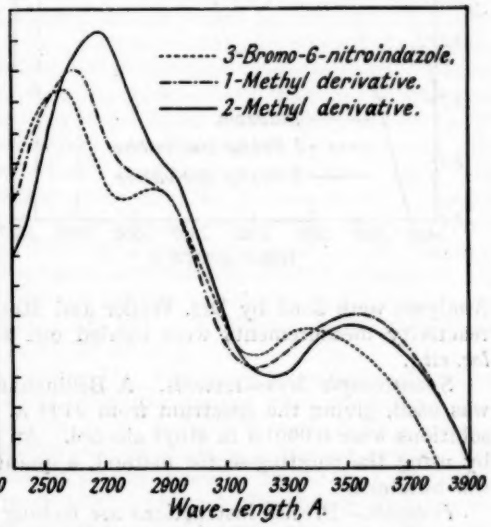
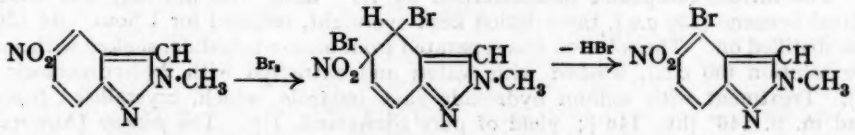


FIG. 2.



derivatives. Little can be deduced from the curves of 6-nitroindazole, but in the other two cases there is a close similarity between the parent indazole and its 1-methyl derivative but a decided difference from the 2-methyl isomer.

Following other workers in the field (*e.g.*, Witt, Noelting, and Grandmougin, *Ber.*, 1890, **23**, 3635), we have assumed throughout that bromination of indazoles occurs in position 3. There is, however, the possibility that, if (say) 5-nitro-2-methylindazole has the quinonoid structure, addition of bromine, followed by elimination of hydrogen bromide (cf. J., 1931, 3308), might occur to give 4-bromo-5-nitro-2-methylindazole (VIII):



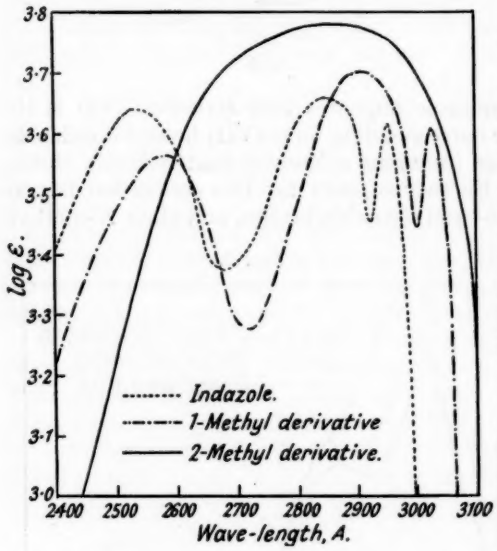
(VIII.)

(The bromine in this compound would be reactive to piperidine and its reactivity would sustain the argument for the quinonoid form.) Formation of the 4-bromo-compound is possible, but in our opinion extremely unlikely in view of the reactive 3-position of indazoles and the presence of the nitro-group in the benzene ring. Further, if bromination did occur preferentially in the 4-position, further bromination to give the 3 : 4-dibromo-compound would be expected. No indication of this was found, although in the several cases investigated excess bromine was used.

Attempts to prepare 5-nitro-1-methylindazole from the methylhydrazone of 2-chloro-

5-nitrobenzaldehyde were unsuccessful. This is rather surprising in view of the ease with which Fries (*loc. cit.*) effected ring-closure of the phenylhydrazone of 2-chloro-5-nitrobenzophenone, though on the other hand Meyer (*Ber.*, 1893, **26**, 1253) could not effect closure of a ring in the phenylhydrazone of 2-chloro-5-nitrobenzaldehyde.

FIG. 3.



Auwers and Duesberg (*loc. cit.*) formulated the rule that alkylation of indazoles in alkaline solution takes place mainly in the 1-position. Exceptions to the rule are known (*e.g.*, Auwers and Dereser, *Ber.*, 1919, **52**, 1340). We have found other exceptions in the methylation of 6-nitroindazole and 3-bromo-6-nitroindazole, and are inclined to doubt the general validity of this rule, as the quantitative separation of the isomers produced is a matter of difficulty.

EXPERIMENTAL.

Unless otherwise stated, the methods of preparation, properties, and purification of compounds used are those given in the literature. The purity of the compounds was checked by the sharpness of their m. p.'s on the Kofler micro-apparatus (*Mikrochem.*, 1934, **15**, 242). Analyses were done by Drs. Weiler and Strauss, Oxford, and Mr. Brown, Edinburgh. The reactivity measurements were carried out as in previous papers (Campbell and McLeish, *loc. cit.*).

Spectroscopic Measurements.—A Bellingham and Stanley "medium" quartz spectrograph was used, giving the spectrum from 2400 A. to the red region on a 10 × 4 in. plate. The solutions were 0·0001M in ethyl alcohol. An iron spark was used as the source of light, and by using the rotating-sector method, a quantitative determination of the absorption curves was obtained.

Indazole.—Precise instructions are lacking for the preparation of indazole by the method of Jacobson and Huber (*Ber.*, 1908, **41**, 2574). The following method was finally adopted (cf. Auwers, *Ber.*, 1919, **52**, 1335; Haworth and Hey, J., 1940, 365). Benz-*o*-toluidide (20 g.) was dissolved in a hot mixture of acetic acid (50 c.c.) and acetic anhydride (50 c.c.) and rapidly cooled with stirring to obtain fine crystals. The mixture was then cooled to 3°, and nitrous fumes passed in at the rate of one or two bubbles per second. A deep green colour was obtained after about 20 mins., the temperature of the solution never having exceeded 10°. Immediately a clear solution was obtained it was poured into water (100 g.) and ice (100 g.). The oil which separated soon solidified on being stirred. The precipitate was washed with cold water until only a faint odour of acetic acid remained, pressed on tile, and dried at room temperature for 2 hours. The nitroso-compound (characterised by its "flash" on heating) was added to sodium-dried benzene (150 c.c.), the solution kept overnight, refluxed for 1 hour, and 100 c.c. of benzene distilled off. The solution was separated from benz-*o*-toluidide, shaken with sodium carbonate solution (50 c.c.), washed with water, and extracted with 2N-hydrochloric acid (100 c.c.). Treatment with sodium hydroxide gave indazole, which, crystallised from hot water, had m. p. 146° (lit., 146°); yield of pure compound, 1 g. The *picrate* (Auwers and Duesberg, *loc. cit.*) crystallised from ether in yellow needles, which were converted into orange prisms on standing in suspension; m. p. 136° (lit., 136—137°). It had not previously been analysed (Found: N, 19·5. $C_{13}H_9O_7N_5$ requires N, 20·2%).

N-Methyl Derivatives of 3-Bromo-4-nitroindazole.—Great difficulty was experienced in preparing 6-nitro-*o*-toluidine required for making 4-nitroindazole. The preparation from 2 : 4 : 6-trinitrotoluene (Tiemann, *Ber.*, 1870, **3**, 218; Beilstein, *ibid.*, 1880, **13**, 243) gave very poor yields of 2 : 6-dinitro-4-aminotoluene, although many modifications of the method were tried, and removal of the amino-group gave only a 5% yield of the nitrotoluidine. Korner and Cortardi (*Atti R. Accad. Lincei*, 1916, **25**, 339) claimed a 60% yield by the reduction but the

promised experimental details were never published. Cohen and Dakin (J., 1902, **81**, 26) could not obtain the amino-compound directly. *o*-Toluic acid was therefore nitrated, and the resulting mixture separated by the rather unsatisfactory method of Scherpenzeel (*Rec. Trav. chim.*, 1901, **20**, 173). p-*Nitrobenzyl* 4-*nitro*-o-*toluate* formed leaflets (acetic acid), m. p. 149° (Found: N, 8·6. $C_{15}H_{12}O_6N_2$ requires N, 8·8%), and p-*nitrobenzyl* 6-*nitro*-o-*toluate*, prisms (alcohol), m. p. 108—114° (Found: N, 9·3%). 6-Nitro-*o*-toluamide gave a poor yield of 6-nitro-*o*-toluidine by the Hofmann reaction, but Curtius degradation of the azide gave good results. The acid chloride of 6-nitro-*o*-toluic acid (11 g.) was dissolved in benzene (100 c.c.), and powdered sodium azide (3 g.) was slowly added, the solution being vigorously shaken. The solution was finally heated gently and then boiled with an equal volume of concentrated hydrochloric acid for 4 hours. The benzene was removed, and the hydrochloride of 6-nitro-*o*-toluidine converted into the base by trituration with concentrated aqueous ammonia; crystallised from alcohol, it had m. p. 91° (lit., 92°); yield, 40%. 4-Nitroindazole was obtained by Noelting's method (*Ber.*, 1904, **37**, 2582). The indazole was methylated by a quicker method than that of Auwers and Frese (*Ber.*, 1925, **58**, 1369). 4-Nitroindazole (4 g.), potassium hydroxide (3 g.), methyl iodide (9 g.), and methyl alcohol (25 c.c.) were heated under reflux for 4 hours, and the solution poured into water. The precipitate obtained was dried on porous plate, dissolved in ether, and separated by the method of Auwers and Frese (*loc. cit.*). 4-Nitro-1-methylindazole, crystallised from light petroleum (b. p. 80—100°), had m. p. 136° (lit., 138—139°); yield, 0·8 g. The 2-methyl compound, crystallised from water, had m. p. 98° (lit., 101—103°); yield, 0·3 g. The methyl derivatives were brominated by suspending them in dilute hydrochloric acid, adding bromine water, and stirring vigorously for ½ hour. The precipitate was washed with water, and crystallised from alcohol. 3-*Bromo*-4-*nitro*-1-*methylindazole* had m. p. 216—220° (Found: Br, 29·4. $C_8H_6O_2N_3Br$ requires Br, 31·2%). There was only sufficient of the 2-methyl isomer, m. p. 195—199°, for the reactivity measurements.

3-*Bromo*-5-*nitroindazole*.—5-Nitroindazole (1 g.) was brominated in dilute hydrochloric acid as above. The precipitate was boiled with water to remove any unchanged nitroindazole, and obtained in colourless, cubic prisms (alcohol), m. p. 221°; it sublimes in the same form; yield, 1 g. (Found: Br, 31·3. $C_7H_4O_2N_3Br$ requires Br, 33·0%).

N-*Methyl Derivatives of* 3-*Bromo*-5-*nitroindazole*.—The 5-nitromethylindazoles, prepared by the method of Fries (*loc. cit.*), were obtained as colourless needles when crystallised from light petroleum (b. p. 80—100°). From the isomer of m. p. 163°, 3-*bromo*-5-*nitro*-1-*methylindazole* was obtained as pale yellow needles (alcohol–acetic acid) or colourless needles (light petroleum, b. p. 80—100°), m. p. 225°; it sublimes in prisms (Found: Br, 30·6. $C_8H_6O_2N_3Br$ requires Br, 31·2%). From the other isomer, m. p. 129°, 3-*bromo*-5-*nitro*-2-*methylindazole* was obtained in yellow needles (alcohol) or pale yellow needles (light petroleum, b. p. 80—100°), m. p. 188°, subliming in cubic prisms (Found: Br, 30·2%).

Attempted Preparation of 5-*Nitro*-1-*methylindazole*.—2-Chloro-5-nitrobenzaldehyde (Erdmann, *Annalen*, 1893, **272**, 153) gave the 2 : 4-*dinitrophenylhydrazone* as orange prisms (tetralin) or needles (methyl alcohol), m. p. 280° (decomp.) (Found: N, 19·1. $C_{13}H_8O_6N_5Cl$ requires N, 19·1%). 2-*Chloro*-5-*nitrobenzaldehydemethylhydrazone* was prepared by heating the aldehyde (0·85 g.), methylhydrazine sulphate (0·7 g.), and crystalline sodium acetate (0·7 g.) in aqueous alcohol for 10 minutes. Water was added, and the precipitate crystallised first from aqueous methyl alcohol and then from light petroleum (b. p. 60—80°); yellow needles, m. p. 121—122°, subliming (Found: N, 20·2. $C_8H_8O_2N_3Cl$ requires N, 19·7%). All efforts to close the ring in this compound with potassium hydroxide were unsuccessful.

N-*Methyl Derivatives of* 6-*Nitroindazole*.—These were prepared from 6-nitroindazole by the method used for the 5-compound. Auwers and Schwegler (*loc. cit.*) obtained only one of the isomers in the pure state. We effected separation of the mixture by fractional crystallisation from methyl alcohol, 6-nitro-2-methylindazole separating from the hot solution in yellow prisms, m. p. 160° (lit. 159—160°). Addition of water to the filtrate gave the 6-nitro-1-methylindazole, which separated as colourless needles from light petroleum (b. p. 60—80°), m. p. 125° (lit., 105—108°) (Found: C, 54·5; H, 3·9. Calc. for $C_8H_7O_2N_3$: C, 54·3; H, 3·9%). The yield of the 2-methyl is three times that of the 1-methyl derivative.

N-*Methyl Derivatives of* 3-*Bromo*-6-*nitroindazole*.—These were prepared either by methylation of 3-bromo-6-nitroindazole (5·0 g.) or by bromination of the 6-nitromethylindazoles by methods given above. In the first case, the isomers were separated by ether. The insoluble isomer was crystallised three times from ethyl alcohol, yellow needles, m. p. 175°; yield 2·5 g. (50%) (Found: Br, 31·6. $C_8H_6O_2N_3Br$ requires Br, 31·2%). As the compound is identical with that obtained by the bromination of 6-nitro-2-methylindazole, it is 3-*bromo*-6-*nitro*-2-*methyl*-

indazole. The soluble 1-*methyl* isomer was crystallised several times from methyl alcohol, forming colourless, elongated prisms, m. p. 156°; it sublimed in compact prisms. Yield 0·7 g. (14%) (Found : Br, 31·5%).

Colour of Nitroindazole Derivatives.—Some of the nitroindazole derivatives are stated in the literature to be coloured (*e.g.*, Fries, *loc. cit.*). It was found, however, that when crystallised from light petroleum most of them were colourless, the exceptions being 3-bromo-5- and -6-nitro-2-methylindazole (both yellow).

We wish to thank several of the advanced students in the Department for preparing intermediates, the Carnegie Trust for the Universities of Scotland for a teaching fellowship to one of us (N. C.), and the Moray Fund for a grant.

UNIVERSITY OF EDINBURGH. [*Received, November 21st,* 1940.]

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27. *Reaction Velocities at Low Temperatures. Part III. The Synthesis of Diethylacetal at Temperatures between − 44° and + 25°.*

By R. P. BELL and A. D. NORRIS.

The kinetics of the formation of acetal in ethyl-alcoholic solution have been studied at six temperatures between −44° and +25° with the hydrogen ion as a catalyst. The course of the reaction obeys the expected laws when the retarding effect of the water produced is taken into account. The values of the catalytic constant at different temperatures can be expressed within the experimental error by the Arrhenius equation, and their order of magnitude agrees with the simple collision theory.

THE formation and hydrolysis of acetals have long been known as examples of acid catalysis, and recent work (Deyrup, *J. Amer. Chem. Soc.*, 1934, **56**, 60) has shown that the formation of acetal from acetaldehyde in ethyl-alcoholic solution takes place at a measurable rate at room temperature at hydrogen-ion concentrations of about 10^{-4}N. In the present work this reaction has been studied at low temperatures with the object of detecting possible deviations from the Arrhenius equation. The catalyst used was hydrogen chloride, which can be assumed to be completely dissociated in ethyl alcohol at the temperatures used.

EXPERIMENTAL.

Materials.—Ethyl alcohol was refluxed for 8 hours over aluminium amalgam and then twice distilled through a 1-m. column; different preparations gave indistinguishable results. Acetaldehyde was freshly distilled in small quantities immediately before use. Hydrogen chloride, prepared from " AnalaR " sodium chloride and concentrated sulphuric acid, was absorbed in alcohol and diluted to the required concentration by weight.

Measurement of Reaction Velocity.—The low-temperature thermostat already described (Bell and Thomas, J., 1939, 1573) was used with a few modifications. When ammonia was used as refrigerant the deposition of calcium carbonate in the water pump during the night was avoided by absorbing the greater part of the ammonia gas in a vessel containing 3 l. of water. It was also found convenient to by-pass the mercury column when refilling with refrigerant. In the present work the temperatures were measured with a platinum resistance thermometer, standardised at the f. p. and b. p. of water, the f. p. of chlorobenzene, and the sublimation point of carbon dioxide. Experiments at 0° were done in ice, and at 25° in an ordinary thermostat.

The reactions were carried out in vessels of the type described by Bell and Levinge (*Proc. Roy. Soc.*, 1935, *A*, **151**, 211) and were started by adding a small quantity of acetaldehyde (which need not be accurately known) from a micro-pipette. The initial acetaldehyde concentration was about 0·02M, and the course of the reaction was followed by extracting from time to time samples of about 0·5 c.c. and determining the acetaldehyde concentration by the method of Friedmann, Cotonio, and Shaffer (*J. Biol. Chem.*, 1927, **73**, 342). A slight modification of the method of estimation is necessary since in an unbuffered solution of bisulphite the acetal formed is hydrolysed back to acetaldehyde at an appreciable rate; on the other hand, if the p_H of the bisulphite solution is too high, the aldehyde–bisulphite compound is formed too slowly. Satisfactory results were obtained by using a solution containing 0·5 mol. of potassium hydrogen

sulphite and 0·05 mol. of sodium hydroxide per l., each sample being left for 30 mins. before titration. The final titration was done with N/100-iodine solution from a micro-burette.

At the low temperatures used there might be complications due to the formation of paraldehyde or metaldehyde. This was tested by hydrolysing with very dilute acid samples at different stages of the reaction and then estimating the acetaldehyde present. Both at −20° and −40° it was found that the quantity of acetaldehyde thus determined did not vary during the reaction. Since neither paraldehyde nor metaldehyde would have been appreciably converted into acetaldehyde under the conditions of hydrolysis employed, this shows that they were not formed at any stage of the reaction.

Calculation of Velocity Constants.—The kinetics of the reaction are complicated by the water produced, which reacts partly with the ion $C_2H_5{\cdot}OH_2^+$ according to the equation

$$C_2H_5{\cdot}OH_2^+ + H_2O \rightleftharpoons C_2H_5{\cdot}OH + OH_3^+ \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where OH_3^+ is much less active as a catalyst than $C_2H_5{\cdot}OH_2^+$. The equilibrium constant for the reaction, $r = [C_2H_5{\cdot}OH_2^+][H_2O]/[OH_3^+]$, has been determined at 25° by Goldschmidt (*Z. physikal. Chem.*, 1907, **60**, 728) and Millar (*ibid.*, 1913, **85**, 129). In order to obtain values for lower temperatures we have made approximate calorimetric measurements of the heat change in reaction (1). Three measurements at 25° gave heat evolutions of 4940, 5290, and 4910 cals./mol., and one measurement at 0° gave 4800 cals./mol. Taking 5000 cals./mol. as a mean value, we obtain the following values for r: 0·15 at +25°, 0·097 at +10°, 0·070 at 0°, 0·034 at −20°, 0·018 at −35°, 0·013 at −44°. It may be noted that values for the corresponding equilibrium constant in methyl alcohol (Smith, *J. Amer. Chem. Soc.*, 1939, **61**, 256) lead to a heat of reaction of 4800 cals./mol.

If the concentration of acid catalyst is small compared with that of acetaldehyde (as was the case at temperatures of −20° and higher) the course of the reaction is given by the equation

$$kt = [(a + r)/r] \log_{10} a/(a - x) - 0{\cdot}434x/r \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where a is the initial concentration of acetaldehyde and x the concentration of acetal after time t. For higher acid concentrations, however, a more complicated expression is necessary. If A is the total acid concentration and y the concentration of OH_3^+ formed after time t, the relevant equations are

$$(A - y)(a - x)/y = r$$
$$dx/dt = 2{\cdot}303\, k_c(a - x)(A - y)$$

where k_c is the catalytic constant of the $C_2H_5{\cdot}OH_2^+$ ion, and it is assumed that catalysis by the OH_3^+ ion can be neglected. The solution of these equations is

$$k_c t + C = \frac{-0{\cdot}434}{A - y} + \frac{A - a - r}{2Ar} \log_{10} \frac{y^2 - (A + a + r)y + Aa}{(A - y)^2}$$
$$+ \frac{(A - a - r)^2 + 4Ar}{4Ar\{\frac{1}{4}(A + a + r)^2 - Aa\}^{\frac{1}{2}}} \log_{10} \frac{y - \frac{1}{2}(A + a + r) + \{\frac{1}{4}(A + a + r)^2 - Aa\}^{\frac{1}{2}}}{y - \frac{1}{2}(A + a + r) - \{\frac{1}{4}(A + a + r)^2 - Aa\}^{\frac{1}{2}}} \quad . \quad . \quad (3)$$

where $2y = A + x + r - \{(A + x + r)^2 - 4Ax\}^{\frac{1}{2}}$ and C is a constant for each reaction. The velocity constants were determined from the experimental data by plotting the right-hand side of equation (2) or (3) against the time, straight lines being obtained within the experimental error.

Results.—The following table gives the velocity constants and catalytic constants obtained at six temperatures. Concentrations are expressed in mols./1000 c.c., and the time in mins. The results at −44° are less accurate than those at higher temperatures, partly because of unsatisfactory temperature control.

	At 25°: $k_c = 84{\cdot}3 \pm 2{\cdot}3$.						
10^5A	2·2	4·3	6·3	10·3	19·9	48·8	
$1000k$	1·86	3·76	5·15	9·68	15·8	38·5	
k_c	84·9	87·0	82·0	93·8	79·3	78·9	
	At 10·13°: $k_c = 21{\cdot}6 \pm 1{\cdot}0$.						
10^4A	0·24	0·36	1·33	2·67	5·33	7·99	10·64
$1000k$	0·42	0·71	2·65	5·84	12·4	19·3	26·2
k_c	17·5	19·5	19·9	21·9	23·3	24·2	24·6

	At 0°: $k_c = 7{\cdot}8 \pm 0{\cdot}4$.						
10^3A	0·50	0·75	1·00	1·04	1·04	3·91	6·01	7·37
$1000k$	3·0	5·9	7·6	7·9	7·0	35·4	53·5	66·0
k_c	6·0	7·8	7·6	7·5	6·7	9·1	8·9	9·0
	At −20·1°: $k = 0{\cdot}84 \pm 0{\cdot}05$.						
10^3A	2·0	3·4	4·0	13·1	16·2	26·2		
$1000k$	1·45	2·71	2·87	12·9	25·8	24·8		
k_c	0·71	0·79	0·71	0·98	0·98	0·95		
	At − 35·1°: $k_c = 0{\cdot}12 \pm 0{\cdot}006$.						
10^3A	0·96	1·28	2·02	2·78	4·37	6·92	10·1	
10^3k	0·94	1·73	2·22	3·89	5·33	7·20	23·5	
$10k_c$	0·98	1·35	1·09	1·40	1·22	1·04	1·34	
	At −44·0°: $k_c = 0{\cdot}036 \pm 0{\cdot}005$.						
10^3A	1·30	2·07	2·47	6·9	8·7	1·07	12·3	15·7
10^4k	2·9	4·2	7·2	35·1	35·6	21·4	87·5	48·6
$100k_c$	2·2	2·0	2·9	5·1	4·1	2·0	7·1	3·1

Discussion.

The mean values for k_c at the six temperatures are expressed excellently by the simple Arrhenius equation. Since the data at −44° are of lower accuracy, the method of least squares was applied to the values for the other five temperatures, giving the equation

$$k_c = 2{\cdot}34 \times 10^{13}\, e^{-15{,}500/RT} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The observed and the calculated value of k_c are given below:

Temp.	25·0°	10·1°	0·0°	−20·1°	−35·1°	−44·0°
k_c obs.	84·3	21·6	7·8	0·84	0·12	0·036
k_c calc.	84·3	21·7	7·85	0·83	0·12	0·034

It will be seen that the agreement is well within the experimental error. The value of the first constant in equation (4) is of the order of magnitude predicted by the collision theory. There is thus no indication of the "tunnel effect," which might be expected to appear at low temperatures in reactions catalysed by acids or bases (Bell, *Trans. Faraday Soc.*, 1938, **34**, 229). Hammett ("Physical Organic Chemistry," pp. 300, 304, New York, 1940) has suggested that in the acetalisation reaction the equilibrium

$$EtOH + Me{\cdot}CHO + \overset{+}{H} \rightleftharpoons Me{\cdot}\overset{+}{C}H{\cdot}OEt + H_2O$$

is set up instantaneously, followed by the slow reaction

$$Me{\cdot}\overset{+}{C}H{\cdot}OEt + EtOH \longrightarrow Me{\cdot}CH(OEt)(\overset{+}{O}HEt)$$

If this mechanism is accepted, no "tunnel effect" would be expected, since the rate-determining step does not involve a proton transfer.

The value we have obtained for the catalytic constant at 25° is about 35% higher than that given by Deyrup (*loc. cit.*), though his value at 35° agrees fairly well with equation (4). It may be noted that the discrepancy at 25° would be accounted for if the alcohol used by Deyrup at this temperature had contained about 0·1% of water. Deyrup also found that added salts had a considerable accelerating effect, and if the hydrogen and chloride ions have a similar effect we might expect k_c to increase with acid concentration at the lower temperatures, where higher concentrations were used. Our experimental results do not provide any evidence for any variation of k_c, which might, however, be masked by the decreased experimental accuracy at lower temperatures. In any case it may be easily seen that the presence of a salt effect of the same order of magnitude as that found by Deyrup would not affect the agreement with the Arrhenius equation, though it would slightly affect the values of the constants.

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Physical Chemistry Laboratory,
Balliol College and Trinity College, Oxford. [*Received, January 7th*, 1941.]

28. *Acridine Syntheses and Reactions. Part I. Synthesis of Proflavine from* m-*Phenylenediamine and its Derivatives.*

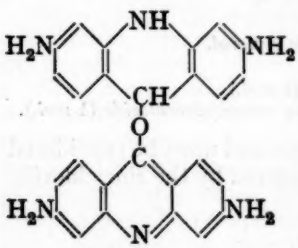
By Adrien Albert.

Processes are described which furnish up to 70% of pure proflavine as the result of a single condensation starting from *m*-phenylenediamine (with oxalic or formic acid), from *m*-amino-oxanilic acid, or from mono (or di)-formyl-*m*-phenylenediamine.

These processes are of general interest, as they enable a variety of simple benzene derivatives to be rapidly converted into derivatives of acridine in good yield. The mechanism of the initial stages of the reaction is discussed.

Although several members of the acridine series have been made by the action of formaldehyde on primary aromatic amines, it is not possible to obtain proflavine (IV) in this way from *m*-phenylenediamine (Meyer and Gross, *Ber.*, 1899, **32**, 2365). The synthesis most often used is that due to Benda (*Ber.*, 1912, **45**, 1787), who nitrated 4 : 4'-diaminodiphenylmethane and heated the product under pressure with stannous chloride, thus obtaining diaminodihydroacridine, which was finally oxidised to proflavine. The patent literature (D.R.P. 347,819; 1921), however, indicated a method that appeared more economical of time and material: *m*-phenylenediamine (1 mol.), glycerol (2 mols.), zinc chloride (1·33 mols.), and oxalic acid dihydrate (1 mol.) are heated for 2 hours at 190°, and a 60% direct yield of proflavine is claimed.

In an attempt to repeat this work, a tarry mass was produced from which proflavine could be isolated with difficulty. However, modification of the process by heating at 155° for 45 minutes and doubling the amount of glycerol gave 55—65% yields of proflavine (exclusive of some 15% lost in purification) and 10% of the *m*-phenylenediamine remained unaltered. No isomeric diaminoacridines could be isolated, the by-products being traces of tar, resinous material, and a pair of related substances, one of which crystallised from alcohol in cream-coloured needles which, when exposed to the air, changed into the other, an orange substance insoluble in alcohol but dissolved by pyridine (green fluorescence) and hydrolysed by hydriodic acid to 2 : 8-diaminoacridine and 2 : 8-diaminoacridone (Albert and Linnell, J., 1936, 88). The orange substance, characterised as its *tetrabutyryl* derivative, is provisionally assigned the constitution, 2 : 8 : 2' : 8'-*tetra-amino*-5 : 10-*dihydrodiacridyl* 5 : 5'-*ether* (I).



(I.)

Although more than half the oxalic acid used in the condensation could be recovered unchanged, a reduction in the amount caused a diminution in yield. Presumably, the excess of oxalic acid acts as a source of hydrogen ions, for this excess can be replaced by an equivalent amount of hydrochloric acid without serious reduction in yield. Although unchanged *m*-phenylenediamine was always found after the condensation, the use of more oxalic acid diminished the yield appreciably, as did excess of mineral acid.

Carbon dioxide began to be liberated at 120° and continued until the condensation was complete, one molecule being liberated for each molecule of proflavine formed.

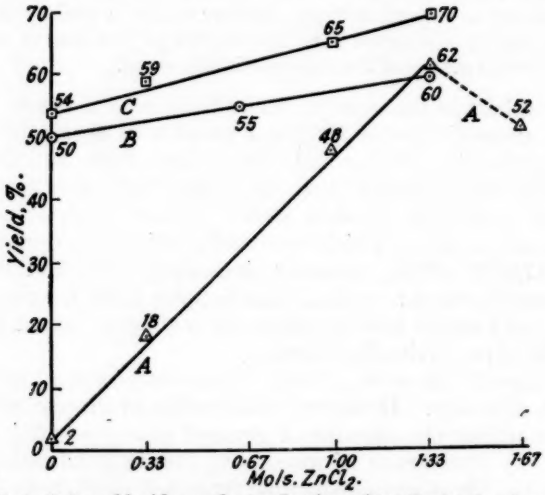
In the condensation, glycerol may be replaced by those alcohols (sorbitol, glycol, 1 : 2-dihydroxypropane) which, containing two adjacent hydroxyl groups, readily convert oxalic acid into formic acid; alcohols which give hardly any formic acid (1 : 3-dihydroxypropane and phenylethyl alcohol) give no proflavine.

The zinc chloride could be replaced by calcium chloride (30% yield) but not by stannous or aluminium chloride. The yield of proflavine fell in linear proportion when the amount of zinc chloride was decreased (see Fig.). This effect is attributed partly to a fall in hydrogen-ion concentration, since both zinc and calcium chlorides evolve hydrogen chloride freely when triturated with oxalic acid. The zinc salt appears in addition to have a specific catalytic action, since, when it is replaced by hydrochloric acid, the yield rises only to 25%.

If zinc chloride is omitted from the reaction, the principal product is *m*-amino-oxanilic acid (III), which is not found during the normal proflavine condensation. Although this

acid might be considered to be the precursor of proflavine, the highest yield obtainable by heating it with *m*-phenylenediamine and hydrochloric acid is only 23%. On the other hand, m-*aminoformanilide* (II) could be isolated from the main reaction by interrupting it at 130° and, when condensed with *m*-phenylenediamine and hydrochloric acid, gave a 70% yield of proflavine.

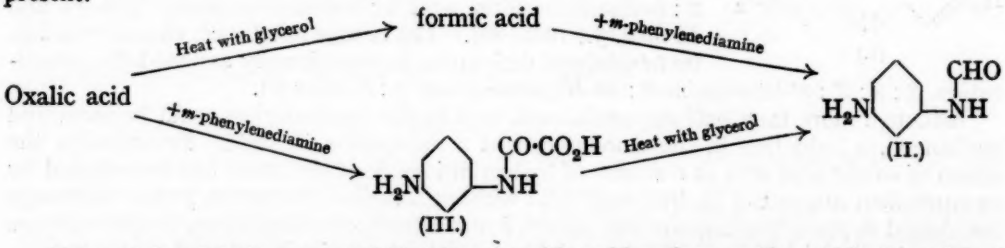
m-Amino-oxanilic acid gave *m*-aminoformanilide (5% at 135°) on warming, but only in the presence of glycerol and mineral acid, so that prior hydrolysis cannot be excluded.



Effect of zinc chloride on the production of proflavine in glycerol.

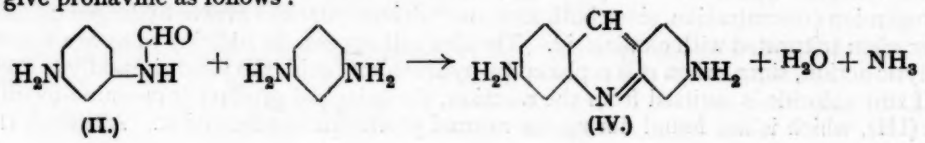
From (A) m-*phenylenediamine* (2 *mols.*) + *oxalic acid* (2 *mols.*),
(B) m-*phenylenediamine monohydrochloride* (2 *mols.*) + *formic acid* (1 *mol.*),
(C) m-*aminoformanilide hydrochloride* (1 *mol.*) + m-*phenylenediamine monohydrochloride* (1 *mol.*).

The reaction up to this point is summarised in the following scheme and must be considered as following principally the upper route, the lower route being hindered by the zinc chloride present.



Although it might be expected that formic acid could replace oxalic acid in the original reaction, zinc chloride, *m*-phenylenediamine, glycerol, and formic acid (even in excess) gave little proflavine when heated together unless hydrochloric acid also was present. As will be seen from the figure (B), the condensation can be effected in the absence of zinc chloride, thus showing that this salt plays its principal rôle in the first stage of the *original* reaction. In the absence of hydrochloric acid, the condensations with formic acid give moderate yields of the diacridyl ether (I).

The *m*-aminoformanilide produced in the original reaction represents only part of the *m*-phenylenediamine taken and apparently condenses with the remainder of this amine to give proflavine as follows:



This reaction, when effected directly by condensing in equimolecular proportions *m*-aminoformanilide (in 95% yield from *m*-nitroformanilide) with *m*-phenylenediamine dihydrochloride and zinc chloride, gave a particularly high yield (70%) of proflavine. The figure (C) shows that zinc chloride does not greatly influence the course of this reaction, which also takes place in the absence of polyhydric alcohols.

m-Aminoformanilide hydrochloride (2 mols.), heated with glycerol and zinc chloride, gave a 60% yield of proflavine, monoformylproflavine probably being produced first. The latter would be a highly labile substance, *diformylproflavine* being completely hydrolysed on contact for a few minutes with cold dilute alkali solution or warm dilute acid. *s*-Diformyl-*m*-phenylenediamine (1 mol.) and *m*-phenylenediamine dihydrochloride (1 mol.) similarly gave a 47% yield of proflavine.

The exact mechanism of the condensation of *m*-phenylenediamine and *m*-aminoformanilide to proflavine is still under investigation. 3 : 3′-Diamino-*N*-formyldiphenylamine has been identified in the reaction mixture, and this substance gives proflavine on heating with acids. However, further evidence favours 2 : 4 : 2′ : 4′-tetra-aminobenzhydrol as the principal intermediate, and this amine is considered to be the source of diacridyl ethers, which are produced in greatest quantity when the reaction mixture contains an excess of formic acid, Kavache (*Ann. Chim.*, 1918, **10**, 236) having shown that formic acid converts benzhydrol into dibenzhydryl ether.

The various condensations described in the experimental part are equally suitable for other diamines and their derivatives (see also Albert and Large, *Nature*, 1938, **142**, 435; Albert, J., 1939, 920).

Experimental.

General.—All the temperatures recorded are internal. Yields, calculated on the amount of amine taken, refer to purified proflavine and disregard unchanged initial material and proflavine lost in purification.

Condensation using Oxalic Acid.—*m*-Phenylenediamine (*v.i.*, 3 g.) was added at 120° to zinc chloride (5 g.; 1·33 mols.), dissolved in glycerol (10 g.; 4 mols.), in a beaker, and the *m*-phenylenediamine zinc chloride broken up. Oxalic acid dihydrate (3·5 g.; 1 mol.) was added, and the temperature raised during 25 minutes to 155° with gentle stirring (carbon dioxide evolved) and maintained for 45 minutes. The melt was treated with 2·5N-sodium hydroxide (80 ml.), and the precipitate extracted with the minimum quantity of boiling N-hydrochloric acid so that resinous material of low basicity remained undissolved. The filtrate was treated with excess of ammonia to remove zinc, and the precipitate extracted with the minimum quantity of dilute acetic acid. This solution was treated with 20% sulphuric acid (¼ vol.) and left in ice for 4 hours. The red crystals of proflavine sulphate obtained were decomposed by ammonia, and the base dried at 120°. Yield, 1·8 g. (62%) (average of ten experiments). Recrystallisation from 400 parts of boiling water or 55 parts of alcohol produced yellow needles which gave no depression of m. p. with proflavine base synthesised from tetra-aminodiphenylmethane or precipitated from the commercial sulphate (B.D.H.), all the samples melting at 277° [288° (corr.)]. For proflavine, the use of a sealed capillary is considered necessary in order to obtain a sharp m. p. preceded by little sintering.

By stopping the above condensation at various stages, the following amounts of proflavine were found: 140°, 1%; after 5 mins. at 155°, 21%; after 30 mins. at 155°, 53%; 45 mins. at 155°, 61%; 75 mins. at 155°, 48% and much tar. Increasing the amount of oxalic acid by 25% lowered the yields to 32%; decreasing the amount by 25% lowered the yield to 33%, and replacement of the *m*-phenylenediamine by its hydrochloride (5 g.) gave rise to diacridyl ethers (*v.i.*) in 15% yield, no proflavine being formed. However, *m*-phenylenediamine (1·5 g.), *m*-phenylenediamine dihydrochloride (2·5 g.) (equalling in all 3 g. of base), zinc chloride (5 g.), glycerol (10 g.), and oxalic acid dihydrate (1·75 g.; 0·5 mol.) reacted slowly to give a 50% yield of proflavine (65 mins. at 155°).

Condensation using m-*Amino-oxanilic Acid.*—*m*-Amino-oxanilic acid monohydrate (*v.i.*, 2·75 g.; 1 mol.), *m*-phenylenediamine (1·5 g.; 1 mol.), hydrogen chloride (1·0 g., 2 mols., as 3·1 ml. of standardised hydrochloric acid), and zinc chloride (5 g.) in glycerol (10 g.), warmed to 155° during 30 mins. and held there for 45 mins., gave a 23% yield. The use of 1 mol. of hydrogen chloride gave 10%, of 3 mols., 12%, and of 2 mols. in the absence of zinc chloride, 12%, yields.

Condensation using Formic Acid.—*m*-Phenylenediamine (3 g.; 2 mols.), hydrogen chloride (1 g., 2 mols., as 3·1 ml. of concentrated hydrochloric acid), and formic acid (0·72 g. of 90%; 1 mol.) were mixed with a cold solution of zinc chloride (5 g.) in glycerol (10 g.), warmed to 155° during 30 mins., and held there for 45 mins. Yield, 60%. Omission of zinc chloride lowered the yield to 50%, replacing glycerol by phenylethyl alcohol gave an 11% yield, and doubling the quantities of both acids gave diacridyl ethers (*v.i.*) but no proflavine.

Condensation using m-*Aminoformanilide.*—*m*-Phenylenediamine dihydrochloride (2·5 g.; 1 mol.) and *m*-aminoformanilide (1·9 g.; 1 mol.) were added to a cold solution of zinc chloride (5 g.) in glycerol (10 g.), and the mixture warmed to 155° during 25 mins. and held there for 40 mins. Yield, 70%. Less tar was formed in this condensation than in the previous cases. The use of 1 mol. and 3 mols. of hydrogen chloride gave 30% and 35% yields respectively.

m-*Phenylenediamine.*—The material used in the above experiments was freshly distilled and preserved over calcium chloride, which retards its decomposition.

m-*Amino-oxanilic Acid.*—The yield (43%) originally obtained by heating *m*-phenylenediamine (1 mol.) and oxalic acid dihydrate (2 mols.) (Jacobs, *J. Amer. Chem. Soc.*, 1917, **39**, 1451) was increased to 70% when glycerol (5 mols.) was added as a solvent (90 mins. at 140°). The product (+ 1 H_2O), recrystallised from 400 parts of boiling water, had m. p. 237° [245° (corr.)].

m-*Aminoformanilide.*—This was obtained from the oxalic acid condensations (5% at 130°, 10% at 140°) and was freed from *m*-phenylenediamine by rubbing with benzene, in which the latter is more soluble. Further supplies were obtained as follows (compare Albert and Ritchie, *Proc. Roy. Soc. N.S.W.*, 1940, **74**, 77): Raney nickel (10 g.), *m*-nitroformanilide (10 g.), and alcohol (200 ml.) were shaken in hydrogen for 2 hours or until absorption was complete; the filtered liquid was concentrated in a vacuum and allowed to crystallise. Yield, 95%. Further purification, when required, was effected by crystallisation from 3 parts of alcohol. The white needles obtained, m. p. 107°, were soluble in 1 part of boiling alcohol, 150 parts of boiling benzene, *ca.* 50 parts of cold water, more soluble in aqueous ammonia, and very sparingly soluble in ether. The solutions readily became supersaturated. The solid was stable in cold air, but was oxidised in warm air (Found: C, 61·8; H, 5·9; N, 20·9. $C_7H_8ON_2$ requires C, 61·8; H, 5·9; N, 20·6%).

Acyl Derivatives of Proflavine.—2 : 8-*Diformamidoacridine* formed yellow crystals, m. p. 251° (decomp.), sparingly soluble (green fluorescence) in alcohol and most other organic solvents (Found: N, 15·6. $C_{15}H_{11}O_2N_3$ requires N, 15·8%). It was soluble in aqueous sodium hydroxide, proflavine being precipitated through hydrolysis within 3 mins., and was completely hydrolysed in 5 mins. by boiling N-hydrochloric acid. The orange hydrochloride was less soluble in water than that of proflavine.

2 : 8-*Dibutyramidoacridine* formed lemon-yellow crystals (dried at 120°), m. p. 265° [275° (corr.)], not raised by recrystallisation from 7 parts of alcohol, to which it imparted an intense green fluorescence. It was very soluble in boiling water, toluene, chloroform, and acetone (Found: N, 12·8. $C_{21}H_{23}O_2N_3$ requires N, 12·9%). The hydrochloride formed a pale yellow solution in water with intense green fluorescence.

2 : 8 : 2′ : 8′-*Tetra-amino*-5 : 10-*dihydrodiacridyl* 5 : 5′-*ether* (I) was best obtained by refluxing *m*-phenylenediamine dihydrochloride (10 g.), formic acid (10 g.), and glycerol (20 g.), the temperature being raised from 130° to 155° during 90 minutes. The bases formed were precipitated with sodium hydroxide, taken up in cold 0·5% sulphuric acid, chilled, filtered from traces of proflavine sulphate, reprecipitated with sodium hydroxide, and extracted with boiling alcohol. The alcohol-insoluble portion was identical with the substance obtained by exposing the cream-coloured needles, which separated from the alcoholic filtrate, to the air for a day. The former was orange in colour and decomposed at 260° (efferv.) (Found for a sample dried at 25° in a vacuum: C, 65·9; H, 5·7; N, 17·9; loss at 120°, 7·9. $C_{26}H_{22}ON_6,2H_2O$ requires C, 66·4; H, 5·6; N, 17·9; H_2O, 7·7%. The corresponding tetrahydro-compound requires C, 66·1; H, 6·0; N, 17·8%. The completely oxidised tetra-aminodiacridyl ether, $C_{26}H_{20}ON_6,2H_2O$, requires C, 66·6; H, 5·2; N, 18·0%). The last compound is apparently formed on keeping (I) for some weeks; it then becomes insoluble in pyridine. The ether (I) formed dark brown salts, more soluble than those of proflavine, giving no colour with nitrous acid (distinction from proflavine), and coupling with β-naphthol to a port-wine colour. Dr. S. D. Rubbo of the University of Melbourne reports that these salts are protein precipitants and have no antiseptic properties.

2 : 8 : 2′ : 8′-*Tetrabutyramido*-5 : 10-*dihydrodiacridyl* 5 : 5′-*ether*, obtained from (I) (0·26 g.), water (1·5 ml.), butyric acid (0·5 ml.), and butyric anhydride (2 ml.) and recrystallised from acetone–ether, formed buff-coloured crystals, m. p. 250° (not sharp), very sparingly soluble

in water, benzene, and ether and tending to oxidise in the air (Found for material dried in a vacuum : N, 11·75. $C_{42}H_{46}O_5N_6$ requires N, 11·8%).

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UNIVERSITY OF SYDNEY. [*Received, July 24th*, 1940.]

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29. *The Chemistry of Galactogen from* Helix Pomatia. l-*Galactose as a Component of a Polysaccharide of Animal Origin.*

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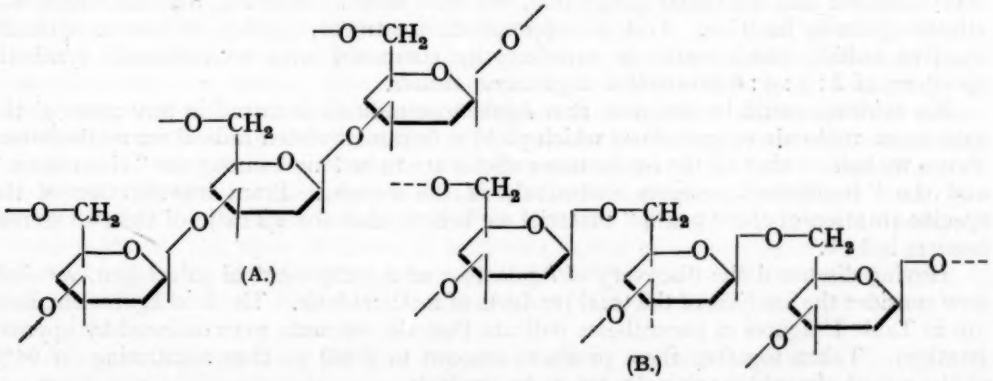
The results discussed in the present communication lead to the following main conclusions : (i) galactogen consists entirely of galactose radicals; (ii) the main part of the galactogen molecule consists of a chain of " backbone " radicals, each carrying a side-chain radical in the manner indicated in formulæ (A) and (B); (iii) for every three backbone radicals there are four side-chain radicals; (iv) the backbone radicals, and together with them three out of every four side-chain radicals, consist of residues of *d*-galactose; (v) one in every four side-chain radicals is derived from *l*-galactose; (vi) the " unit " of structure in galactogen probably comprises seven galactose radicals, and the colloidal properties of the polysaccharide may be due to the aggregation of a number of these 7-radical units.

Galactogen thus appears to be unique in containing radicals derived from both *d*- and *l*-galactose. The latter sugar, so far as we are aware, has not hitherto been detected in material of animal origin.

IN a preliminary study (Baldwin and Bell, J., 1938, 1461) we found that methanolysis of approximately fully methylated galactogen gives rise to dimethyl and tetramethyl methyl-galactosides in roughly equimolecular proportion. We identified the former as 2 : 4-dimethyl methyl-*d*-galactoside and, having at the time no evidence to the contrary, the latter was identified as 2 : 3 : 4 : 6-tetramethyl methyl-*d*-galactoside. We suggested two provisional formulations of the galactogen molecule possessing as their main feature a " backbone " consisting of triply substituted galactose radicals, each of which carried as " side chain " a glycosidically linked galactose radical. The backbone radicals might be linked in either of two ways, (A) in the 1 : 3 position, the side chains being attached glycosidically at C_6, or (B) in the 1 : 6 position with side chains at C_3, but we have as yet no evidence which points specifically to either of these possibilities.



(A.)

(B.)

May (*Z. Biol.*, 1934, **95**, 277) observed that, if galactogen is hydrolysed with hot dilute mineral acid, the final $[\alpha]_D$ of the hydrolysate is + 53·6° (calculated in terms of hexose) as against the + 80·5° expected for an equilibrium mixture of α- and β-*d*-galactopyranoses. Estimations of the galactose contents of these hydrolysates indicated that complete

hydrolysis had been achieved and that no other sugar was present. May concluded that he had to deal with β-*d*-galactopyranose, for which $[\alpha]_D = +53°$, stabilised in some manner hitherto unknown. Carefully repeating May's experiment, we found a final $[\alpha]_D$ value of +56·5° (corr. for ash and calc. in terms of hexose). This is in close agreement with the value of +57·5° which may be calculated for a mixture of *d*- and *l*-galactopyranoses in the proportion of 6 : 1. Other experiments gave values in similarly good agreement with such a ratio.

Using a "galactose-trained" yeast, we attempted to remove *d*-galactose from hydrolysates of galactogen in the hope of isolating some of the *l*-sugar, but in this were unsuccessful. Later, however, we obtained evidence for the presence of 2 : 3 : 4 : 6-tetramethyl methyl-*l*-galactosides in material obtained by the methanolysis of methylated galactogen.

We accordingly resumed our search for *l*-galactose in acid hydrolysates of the parent polysaccharide, this time with the aid of purely chemical procedure. Galactogen was hydrolysed by aqueous hydrochloric acid; from the hydrolysate several crops of *d*-galactose crystallised. The uncrystallisable syrup remaining had only a small positive rotation; from it we prepared by the procedure of Moore and Link (*J. Biol. Chem.*, 1940, **133**, 293) 2-dl-*galactobenziminazole* identical in its properties with material similarly prepared from authentic *dl*-galactose. This isolation of a derivative of *dl*-galactose proves without doubt that the *l*-sugar occurs as a component of the polysaccharide.

At the time of our original experiments we had no criteria wherewith to establish the homogeneity of a small sample of 2 : 3 : 4 : 6-tetramethyl αβ-methyl *d*-galactoside, the few records of physical data in the literature being incomplete and in poor agreement (cf. Bell, J., 1940, 1543). Our sole guide was the preparation of the crystalline anilide, which, in the instance referred to, afforded no evidence of the presence of any but *d*-galactose derivatives. In order to obtain the necessary data one of us (Bell, *loc. cit.*) undertook an investigation of the $n_D^{16°}/[\alpha]_D$ relationship in mixtures of 2 : 3 : 4 : 6-tetramethyl α- and β-methyl-*d*-galactosides along the lines of that already established for the glucose series by Hirst and Young (J., 1938, 1247).

When, in the light of these new data (as already mentioned above) we examined the "pentamethyl" fractions from methylated galactogen, we found that they possessed specific rotations considerably smaller than was to be anticipated from their refractive indices. Analytically, however, the materials were pentamethyl hexose. Having then shown that *l*-galactose radicals were actually present in galactogen itself, we considered the possibility of their methylated derivatives being constituents of the "pentamethyl" fractions. That this was indeed the case was established by hydrolysing the "penta" material and then carefully methylating the product with Purdie's reagents, whereby a large proportion of the β-galactoside was formed. By a procedure involving fractional crystallisation and fractional distillation, we were able to isolate a fraction which was almost optically inactive. This, on appropriate treatment, yielded an almost optically inactive anilide which could be satisfactorily compared with an authentic synthetic specimen of 2 : 3 : 4 : 6-*tetramethyl* dl-*galactose anilide*.

No evidence could be obtained that *l*-galactose radicals occurred in any parts of the galactogen molecule except those which yield a tetramethylated radical on methylation. Hence we believe that all the *l*-galactose radicals are to be found among the "side chains" and the "backbone" consists exclusively of the *d*-sugar. From investigation of the specific rotation of the "penta" material we believe that the *d*/*l* ratio of the two stereoisomers is 3 : 1.

Having discussed the discovery of *l*-galactose as a component of galactogen, we shall now consider the analysis of the total products of methanolysis. The final figures obtained are in Table I (figures in parentheses indicate that the amounts were deduced by approximation). Taken together these products amount to 8·362 g., thus accounting for 94% of the mixed glycosides originally taken for analysis.

Of these products the "penta" and "tri" substances must have originated respectively in the singly substituted side-chain radicals and the triply substituted backbone radicals of the parent polysaccharide. As will be pointed out, we consider that the mixed "tetra" substances originated in potentially "penta"-yielding (*i.e.*, side-chain)

TABLE I.

Composition of methanolysis fractions.

Fraction.	"Penta," g.	"Tetra," g.	"Tri," g.	Total, g.
V	2·545	—	—	2·545
VI	1·430	—	—	1·430
VII	(0·408)	(0·240)	—	0·648
VIII	—	(0·276)	(0·069)	0·345
C	—	(0·092)	(0·584)	0·676
A	—	—	0·590	0·590
IV	—	—	2·128	2·128
Totals	4·383	0·608	3·371	8·362

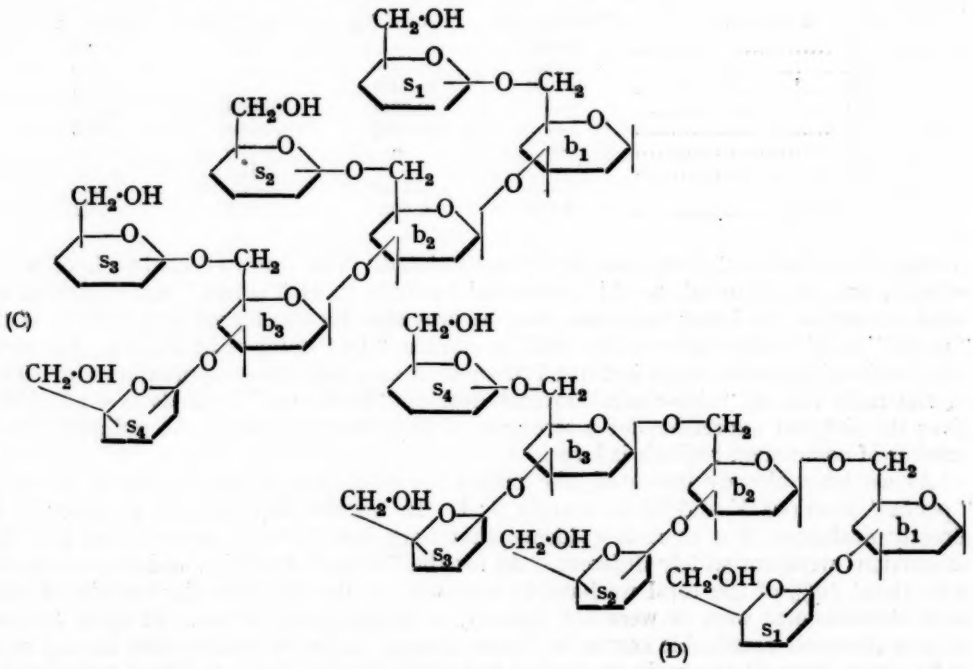
groups which had not been completely methylated. The "tetra" material, of which 0·608 g. was found in all, would correspond to 0·644 g. of "penta" material, and the total amount of the latter must therefore be provisionally considered as 5·027 g. If the "penta" total is thus taken to be 5·027 g. and the "tri" total to be 3·371 g., the molecular ratio of these fractions is 2·01 : 1·52 or 4 : 3 as a very close approximation. That is, the ratio No. of "side-chain" radicals/No. of "backbone" radicals is 4 : 3, which gives the simplest expression for a structure of the galactogen molecule, unless the total number of component radicals is large.

As we have already indicated, the proportion of *d*- and *l*-isomers among the main "penta" fractions V and VI is exactly 3 : 1. In fraction VII this ratio could not be directly evaluated, but there is evidence that both isomers were present and that the proportions were not widely different. As for the "tetra" material, which accounts for only about 10% of the total we have to consider, we do not know for certain whether both stereoisomers were or were not present, or in what proportion. In these circumstances the most reasonable course to follow appears to be to assume that the *d*/*l* ratio of 3 : 1 prevailing in the main fractions (derived from side-chain radicals) prevails also in the subsidiary fractions. As has been already stated, consideration of the final $[\alpha]_D$ attained in acid hydrolysates of galactogen also indicates, for the whole molecule, a *d*/*l* ratio of 6 : 1. Then, since for every three backbone radicals four side-chain radicals are present, one of the latter being derived from *l*-galactose, we reach the conclusion that the molecular unit of galactogen contains a total number of radicals equal to 7 or to some multiple of 7 and, moreover, that one out of every seven radicals is derived from *l*-galactose, the remainder arising from the *d*-sugar.

The basic structures represented in formulæ (A) and (B) suggest several possible arrangements of the galactose radicals. The backbone radicals might constitute a closed loop. In this case the side-chain/backbone ratio would be 1 : 1 instead of the 4 : 3 found. (The 1 : 1 ratio would also occur if the backbone radicals form a very long open chain, each member of which carries a single side chain.) One of the backbone radicals must therefore carry two side chains. The radical in question must be terminally situated in the backbone, for if a second side chain were attached to any intermediate backbone radical, we should expect to find a monomethyl methylgalactoside among the products of methanolysis of the methylated polysaccharide, but we have not found such a product. If, moreover, the terminal backbone radical carried only a single side chain, it would give rise to a trimethyl methylgalactoside, and in this case we should be able to distinguish between (A) and (B), since the terminal backbone radical of the former would be expected to yield 2 : 3 : 4-trimethyl methylgalactoside and that of the latter to yield the 2 : 4 : 6-compound. The small amounts of trimethyl methylgalactosides actually found consisted, however, of more than one isomer.

We must thus conclude, provisionally, that it is the terminal radical of the backbone to which the additional side chain is attached, so, if we picture the molecular unit of galactogen in the simplest possible terms compatible with the evidence, *i.e.*, as containing seven galactose radicals in all, it may be formulated as in (C) or (D). In these formulæ b_1—b_3 represent the backbone radicals and s_1—s_4 those constituting the side chains. With the exception of one of the latter, all these radicals are derived from *d*-galactose.

We have no further evidence regarding the position occupied by the single *l*-galactose radical, beyond the fact that it is one of the side chains.



In both these formulæ a reducing group is represented as being present in the initial backbone radical, b_1, but galactogen possesses only the feeblest of reducing power. The presence of such a reducing group in a 7-radical unit might, however, by analogy with the case of starch, be expected to lead to the polymerisation of a number of such units to form larger colloidal aggregates. Hirst and Young (J., 1939, 1471) have written: " consideration of the conditions of the disaggregation process leads to the conclusion that in the starch molecule, the repeating units . . . are linked to a non-terminal glucose residue of another unit by primary valencies of the glycosidic type." If we suppose, for example, that in the case of galactogen aggregation is brought about by the formation of linkages between the " reducing group " of one 7-radical unit and a hydroxyl group of a side-chain radical of a second such unit, the particular hydroxyl group involved being selected at random, then methylation and subsequent methanolysis would yield " penta," " tetra," and " tri " products in proportions which would vary according to the number of times the inter-unit linkage was repeated in the parent molecule. The proportions can readily be calculated and for the simplest case of polymerisation, in which only two 7-radical units are concerned, the theoretical ratios are 7 : 1 : 6.

It so happens that our actual yields of " penta," " tetra," and " tri " materials correspond to molecular ratios of 1·75 : 0·256 : 1·52, or very nearly 7 : 1 : 6, but this must be a coincidence. Nevertheless it serves to remind us that the " incompletely methylated side-chain radicals," to which we have so far attributed the formation of the " tetra " products, may have failed to undergo complete methylation for one of two reasons, either (*a*) because the original methylation procedure was not sufficiently vigorous or (*b*) because they were in fact involved in inter-unit linkages of the kind just suggested and therefore not susceptible of methylation in any case. Definitely to establish the nature of the inter-unit linkages and the number of these present in the complete galactogen molecule would require material far in excess of the amounts at present at our disposal, but we hope to be in a position to carry out further work on the problem at some future time.

Experimental.

Throughout the work solvents were evaporated under reduced pressure. Polarimetric observations were made in a 2 dm. tube.

Isolation of 2-dl-*Galactobenziminazole from a Galactogen Hydrolysate.*—7·475 G. of galactogen were hydrolysed with 1% hydrochloric acid on the boiling water-bath for 7 hrs. The hydrolysate was neutralised with silver carbonate, filtered, treated with hydrogen sulphide, filtered through charcoal and kieselguhr, and evaporated nearly to dryness. The residue was dissolved in boiling 90% alcohol, decolorised with charcoal, and again filtered. From the solution six crops of crystalline material were obtained: these had the following properties after recrystallisation, and consisted of practically pure *d*-galactose:

Crop No.	Wt., g.	Initial $[\alpha]_D$ (extrapolated).	Final $[\alpha]_D$.	M. p.	M. p. mixed with *d*-galactose.
1	1·670	+144°	+77·7°	162°	162—163°
2	0·629	+141	+76·3	160	160—163
3	0·200	+141	+77·2	160	160—162
4	0·325	+140	+74·0	161	161
5	0·285	+132	+74·9	161	160—162
6	0·273	+148	+75·3	162	160—162

The residual syrup was decolorised with charcoal in aqueous solution and the residue remaining after filtration and evaporation of the filtrate was dissolved in boiling 97% alcohol. Some syrup separated on cooling; this was rejected and the material remaining in the mother-liquor was recovered by evaporation to dryness. The residue showed $[\alpha]_D$ + 11·5°, corresponding to a mixture of approximately 57% of *d*-galactose with 43% of the *l*-isomer (or about 86% of *dl*- and 14% of *d*-galactose).

This material was submitted to the procedure described by Moore and Link (*loc. cit.*) for the preparation of benziminazole derivatives of hexoses. The product crystallised from hot water in prisms (Found: C, 53·3; H, 6·4; N, 10·0. $C_{13}H_{16}O_5N_2$ requires C, 53·7; H, 6·0; N, 10·4%). In crystalline form and m. p. it differed from the derivative of *d*-galactose (Moore and Link, *loc. cit.*). It was optically inactive in 5% aqueous citric acid (*c*, 2·5) and had m. p. 233°, not depressed by authentic 2-dl-*galactobenziminazole* (m. p. 233°) prepared from *dl*-galactose (Found: C, 53·5; H, 6·3; N, 10·4%). From the material obtained from galactogen, a second crop of crystals was obtained by evaporation of the mother-liquor from the first crop, but this was almost entirely the *d*-compound; the *dl*-derivative is sufficiently insoluble to crystallise almost completely in the first crop.

Preparation of Methylated Galactogen.—Our galactogen was prepared from albumin glands taken from hibernating specimens of *H. pomatia* by the method already described (Baldwin and Bell, *loc. cit.*). Acetylation again proved very difficult of accomplishment, but the final product could not be noticeably fractionated by precipitation with light petroleum from its solution in chloroform.

Methylated galactogen was prepared by treatment of the acetate with 30% caustic soda solution and methyl sulphate, the method being essentially the same as that already described. After 16 treatments with these reagents a methoxyl content of 41·8% was attained, and the product then purified by repeated precipitation from solution in chloroform by the addition of light petroleum.

Methanolysis of Methylated Galactogen.—Preliminary fractionation of the products. 9·0 G. of the methylated polysaccharide were boiled for 10 hrs. with 500 ml. of methyl alcohol containing 5 g. of dry hydrogen chloride. After neutralisation with lead carbonate the solution was filtered and evaporated to dryness, and the residue exhaustively extracted with ether containing 10% of acetone. All organic material was in this way extracted. The extract was boiled with charcoal, filtered, and evaporated to dryness; the pale yellow syrup (8·90 g.) obtained was fractionally distilled in a high vacuum, giving fractions I—IV and a still residue, *A*. The properties of these and the later fractions are summarised in Table II.

Fractions I and II were united and redistilled, giving two fractions, V and VI, and a still residue, *B*. The last was united with the partly crystalline fraction III and the whole redistilled to give fractions VII and VIII and a still residue *C*.

Investigation of the "penta"-fractions (V *and* VI): *Isolation of sub-fractions containing tetramethyl* l-*galactose.* Fraction V obviously consisted wholly of pentamethyl hexose, but consideration of the $n_D^{16°}/[\alpha]_D$ relationship (Bell, *loc. cit.*) showed that tetramethyl α- and β-methyl-*d*-galactopyranosides could not be the sole constituents, since the $n_D^{16°}$ found corresponded to an $[\alpha]_D$ of about + 90°, the value actually observed being, however, + 47·5°.

TABLE II.

Properties of the Methylated Fractions.

Fraction.	Wt., g.	B. p./mm.	$n_D^{16°}$.	$[\alpha]_D$ in water.	% OMe.
I	3·177	120—130°/0·08	1·4513	—	—
II	1·719	130—140/0·08	1·4535	—	—
III	1·155	140—166/0·08	1·4644	—	—
IV	2·128	166—175/0·08	—	—	—
A	0·590	—	—	—	—
V	2·545	110/0·001	1·4490	+47·0° (*c* = 5); +47·5° (*c* = 8·7)	60·7
VI	1·430	110/0·001	1·4494	+55·6° (*c* = 2·7)	61·0
B	—	—	—	—	—
VII	0·648	120/0·005	1·4560	—	53·0
VIII	0·345	145/0·005	1·4600	—	49·5
C	0·676	—	—	—	—

Similarly fraction VI, also wholly "pentamethyl," had $[\alpha]_D$ + 55·6°, much lower than the + 118° anticipated from the $n_D^{16°}$ observed. On the assumption that these fractions are derived from a mixture of the *d*- and the *l*-form of galactose, fraction V would correspond to a mixture of 76% of the *d*- and 24% of the *l*-, and fraction VI would correspond to a mixture of 73% of *d*- with 27% of the *l*-component. These fractions were further investigated in the following manner.

They were united and 2·697 g. hydrolysed with 40 ml. of N-hydrochloric acid to give the free sugars. The hydrolysates were neutralised with barium carbonate, filtered, and evaporated to dryness. The free sugar was extracted from the residue with a small quantity of light petroleum (b. p. 60—80°), from which, after evaporation of the solvent, 2·029 g. of a colourless syrup were obtained. This material had $[\alpha]_D$ in water + 37·2° (*c* = 4·8). 2 : 3 : 4 : 6-Tetramethyl *d*-galactose has $[\alpha]_D$ + 117·8° at equilibrium. If, therefore, our material consisted of a mixture of the *d*- and the *l*-derivative, its $[\alpha]_D$ would correspond to a mixture of 66% of the *d*- and 33% of the *l*-isomer. Presumably some of the *d*-material had been left behind in the barium residues on account of its greater relative insolubility, as compared with the *dl*-compound.

The free sugar was now carefully methylated with Purdie's reagents, and the product very slowly distilled in a high vacuum. Two fractions were collected and found to have identical properties. Both crystallised. They were united, and the crystals drained on porous tile for 3 hrs. at 0° and then for 12 hrs. at room temperature. Three recrystallisations at about 3° from light petroleum (b. p. below 40°) gave 42 mg. of fine needles having the properties of pure 2 : 3 : 4 : 6-tetramethyl β-methyl-*d*-galactoside, namely, m. p. 47—49°, $[\alpha]_D$ in water + 18·9° (*c* = 1·4) (cf. the constants given by Bell, *loc. cit.*). A mixture with authentic material showed no depression of m. p.

The still residue from the last distillation also crystallised, and after draining on porous tile and recrystallisation from light petroleum 77 mg. of needles, m. p. 43—44°, were obtained. This sub-fraction (*X*) had very small optical activity, however, showing $[\alpha]_D$ in water + 1·2° (*c* = 2·6), corresponding to a mixture of about 53% of *d*- and 47% of *l*-tetramethyl αβ-methyl-galactosides.

The material absorbed by the tiles used in the above operations was extracted with ether. After evaporation of the solvent, the crystals which remained were drained on porous tile and twice recrystallised; the m. p. was then 39—41°. The substance had $n_D^{16°}$ 1·4486 and $[\alpha]_D$ in water + 25·4°: from the $n_D^{16°}/[\alpha]_D$ relationship this corresponded to a mixture of 72% of the *d*- and 28% of the *l*-isomer. Crystallisation from more than the minimum quantity of solvent, kept at 20°, yielded a second sub-fraction (*Y*), m. p. 42°, $[\alpha]_D^{20°}$ + 0·5° (water; *c* = 1·0).

No further purification of *X* and *Y* was possible on account of the exceptional solubility of the pentamethyl hexose in all solvents. United, these sub-fractions amounted to about 100 mg., which were hydrolysed by hot 5% hydrochloric acid to the free sugar, and then subjected to anilide formation in the usual way. The fine needles (70 mg.) obtained, when recrystallised from alcohol or ethyl acetate, had m. p. 179—181° and $[\alpha]_D$ in acetone (uncatalysed), − 2° (*c* = 2) (Found: C, 61·7; H, 8·3; N, 4·4; OMe, 39·3%). A mixture with 2 : 3 : 4 : 6-tetramethyl *d*-galactose anilide melted at 179—197°. A mixture with synthetic 2 : 3 : 4 : 6-tetramethyl *dl*-galactose anilide (prepared as described below) showed no depression.

2 : 3 : 4 : 6-*Tetramethyl* dl-*galactose anilide* was prepared in the following manner. 1·2 G. of pure *dl*-galactose were boiled for 6 hrs. with 25 ml. of methyl alcohol containing 1% of dry hydrogen chloride. The product (1·2 g.), a glass, isolated in the usual way, possessed no reducing properties and was optically inactive. It was methylated once by the methyl sulphate

method and once with Purdie's reagents, 0·9 g. of a colourless syrup being obtained. This had the properties of tetramethyl methyl-*dl*-galactoside, *viz.*, $n_D^{16°}$ 1·4502; $[\alpha]_D$ in water, zero ($c = 3·21$); OMe, 60·0%. This product was hydrolysed by boiling with 5% hydrochloric acid, and the free sugar isolated in the usual way. It was optically inactive in water ($c = 5·0$) and had OMe, 51·0%. 0·7 G. of this sugar was boiled with 0·7 g. of aniline and 10 ml. of 97% alcohol for 5 hrs. On evaporation a crystalline residue remained. The new substance was recrystallised from alcohol or ethyl acetate until a constant m. p. of 179—180° was attained; yield, 0·45 g. A mixture with 2 : 3 : 4 : 6-tetramethyl *d*-galactose anilide melted at 179—197°. The substance was optically inactive in acetone ($c = 2·5$) (Found: C, 61·7; H, 8·7; N, 4·6; OMe, 39·2. $C_{16}H_{25}O_5N$ requires C, 61·7; H, 8·0; N, 4·5; OMe, 39·9%).

There appears to be no doubt that the anilide obtained from the crystalline sub-fractions *X* and *Y* derived from fractions V and VI consists of tetramethyl *dl*-galactopyranose anilide, mixed with a small proportion of the *d*-isomer. Since Haworth and Leitch (J., 1913, **113**, 188) record $[\alpha]_D$ in acetone (uncatalysed), − 83·3° for the latter substance, the value found, − 2°, corresponds to the presence of about 2—3% of the *d*-anilide. The evidence afforded by the m. p. and mixed m. p. determinations agrees with this conception.

Investigation of fraction IV. 2·010 G. of the hard crystalline mass to which this distillate rapidly set were hydrolysed by boiling with N-hydrochloric acid in the usual manner. After the acid had been neutralised with silver carbonate, the solution was filtered before and after passage of hydrogen sulphide and evaporated to dryness. The bulk of the residual syrup, 1·75 g. (95% yield), crystallised at 37° from moist ethyl acetate–alcohol, yielding several crops of 2 : 4-dimethyl galactose monohydrate, m. p. 104—106°, $[\alpha]_D$ in water (at equilibrium) + 85·0° ($c = 4·5$). Smith (J., 1939, 1724) gives + 85° and + 87·5° and later (J., 1940, 1035) + 86° for the specific rotation of this compound.

The dried syrupy residues remaining after the above crystallisations weighed 400 mg. and had $[\alpha]_D^{22°}$ in water + 93·4° ($c = 3·1$). The above value of + 85·0° for the monohydrate corresponds to + 92° for the anhydrous sugar. This indicated that no appreciable amount of derivatives of *l*-galactose occurs among the " trimethyl " fraction.

300 Mg. of the syrup were boiled with 0·4 ml. of aniline and 5 ml. of alcohol for 4 hrs. The crystalline residue obtained on evaporation of the solution to dryness was recrystallised from alcohol (yield, 110 mg.); it had m. p. 216°, not depressed by authentic 2 : 4-dimethyl *d*-galactose anilide, $[\alpha]_D$ in pure, dry pyridine, − 180° ($c = 1·5$). 300 Mg. of authentic 2 : 4-dimethyl *d*-galactose, under identical conditions of anilide formation, yielded 285 mg. of pure anilide, $[\alpha]_D$ in pyridine, − 181°; Hirst and Jones (1939) give a value of − 174°. Fraction IV therefore consisted almost wholly of 2 : 4-dimethyl αβ-methyl-*d*-galactoside. No contaminant could be detected.

Investigation of residue A. This consisted of 590 mg. of a hard brown glass containing some crystals. It was boiled for 4 hrs. in methyl alcohol containing 1% of dry hydrogen chloride. After neutralisation with silver carbonate, filtration, etc., the residue crystallised from ether containing a little acetone to yield 490 mg. of 2 : 4-dimethyl αβ-methyl-*d*-galactosides (OMe, 41%). This was confirmed by hydrolysis to the free sugar, followed by anilide formation, 400 mg. of product being obtained, m. p. alone or mixed with authentic anilide, 215°; $[\alpha]_D$ in pyridine, − 181°.

From the crystallisation of the mixed dimethyl galactosides a dark coloured residual syrup (120 mg.) remained. Beyond showing that it approximated in composition to a trimethyl hexose, we did not further investigate it. Residue *A* thus consisted essentially of 2 : 4-dimethyl methyl-*d*-galactosides (or polymerisation products).

Investigation of fraction VII. This fraction (648 mg.) had OMe 53%, a value which might be approximately afforded by either of the following mixtures of methylated hexosides: (*a*) 30% of " pentamethyl " with 70% of " tetramethyl " (*b*) 63% of " pentamethyl " with 37% of " trimethyl." In an endeavour to decide between these possibilities, 600 mg. of the material were hydrolysed to the free sugar in the usual way, and the crude product extracted with ether. The syrup (490 mg.) obtained by removal of the solvent was subjected to anilide formation and 500 mg. of fine needles were obtained on crystallisation from alcohol. Although these were superficially identical with the anilide of 2 : 3 : 4 : 6-tetramethyl *d*-galactose, the m. p. was considerably lower, *viz.*, 178°. No other crystalline substance could be detected. The methoxyl content of the crystals (Found: OMe, 39·1. Calc. for tetramethyl hexose anilide: OMe, 39·8%) indicated that this anilide was derived from a tetramethyl hexose, and since the presence of derivatives of *l*-galactose had been discovered in the " pentamethyl " fractions it seemed likely that the product under discussion was a mixture of the *d*- and the

l-tetramethyl galactose anilide. Haworth and Leitch (*loc. cit.*) state that the specific rotation in acetone of 2 : 3 : 4 : 6-tetramethyl *d*-galactose anilide is initially − 83·3°, rising to + 40·7°. Our material showed $[\alpha]_D$ in acetone, − 59·7°, remaining constant for 60 minutes, but on catalysis with a trace of hydrogen chloride it rose to a constant value of + 28·2° in 10 minutes. The initial value corresponds to a ratio of *d*/*l*-components of 86 : 14 and the final value to a ratio of 87 : 13. From the yields of tetramethyl *d*- and *l*-galactose anilides obtained in this experiment it would appear that fraction VII consists of tetramethyl methyl-*d*- and -*l*-galactosides (63% or 0·408 g. approx.) together with trimethyl methylgalactoside (37% or 0·240 g. approx.), and possibly a little dimethyl methylgalactoside.

Investigation of fraction VIII. This amounted to 345 mg., of which 320 mg. were hydrolysed to the free sugars and condensed with aniline in the usual way. The crude product consisted in part of very fine needles (50 mg.); recrystallised from ethyl acetate, these had m. p. 180°. A mixture with authentic 2 : 4 : 6-trimethyl *d*-galactose anilide (Hirst and Jones, J., 1939, 1482) showed no depression, whereas a mixed m. p. with material from fraction VII was 155—165°. The crystalline form of the anilide is very characteristic; no sign of the plate-like crystals of the 2 : 3 : 4-isomer (Hirst and Jones, *loc. cit.*) could be detected. 2 : 3 : 6-Trimethyl galactose does not form a crystalline anilide, and the derivative, if any, of 3 : 4 : 6-trimethyl galactose is unknown. Our material showed mutarotation in acetone (catalysed by a trace of hydrogen chloride) from $[\alpha]_D$ − 96·1° to + 40·0° in 120 minutes (c = 1·32); Hirst and Jones report values of from − 92° to + 38° for 2 : 4 : 6-trimethyl galactose anilide.

Apart from a few mg. of 2 : 4-dimethyl *d*-galactose anilide, no identifiable substance was obtained from the residues remaining after the above crystallisation. The methoxyl content (49·5%) of fraction VIII, together with its position in the distillation sequence, indicated that it must consist approximately of 80% of " tetramethyl " and 20% of " trimethyl " material, *i.e.*, about 276 mg. and 69 mg. respectively. Since a 70% yield of strongly crystallising anilide may be expected from 2 : 4 : 6-trimethyl galactose, and our yield was only 50 mg. instead of the 235 mg. to be expected, only some 20% of the tetramethyl fraction consisted definitely of 2 : 4 : 6-trimethyl methyl-*d*-galactoside.

It seems probable that the small amounts of " tetramethyl " material present in fractions VII and VIII consisted of a mixture of several isomers, although only one of these could be identified. It is therefore likely that the heterogeneous " tetramethyl " substances had their origin in incomplete methylation of some of the side-chain radicals of the original galactogen, rather than in the presence in that polysaccharide of a typical " end-group." Such a group would be expected to give rise to a single trimethyl methylgalactoside.

Investigation of residue C. This was partly crystalline and weighed 676 mg. It was repeatedly extracted at room temperature with large volumes of light petroleum (b. p. 60—80°). The residue (490 mg.) had $n_D^{16°}$ 1·4757 and OMe 40·1%. This was hydrolysed to the free sugar, from which a crystalline anilide was obtained in good yield. This proved to be 2 : 4-dimethyl *d*-galactose anilide, m. p. 214—216°, alone or mixed with authentic material. This portion must thus have consisted almost entirely of 2 : 4-dimethyl αβ-methyl-*d*-galactosides. The petroleum extracts were evaporated to dryness and yielded 184 mg. of a syrup with $n_D^{16°}$ 1·4658 and OMe 46%. These figures and the position in the distillation sequence suggest that it consisted of approximately equal parts of " tetra " and " tri " materials. Hydrolysis to the free sugar, followed by condensation with aniline, failed to yield any identifiable material.

Residue *C* thus approximated in composition to a mixture of 92 mg. of trimethyl methyl-galactoside (probably mixed *d*- and *l*-isomers) with 584 mg. of 2 : 4-dimethyl methyl-*d*-galactoside.

We wish to thank Mr. S. Williamson for preparing the *dl*-galactose used in this investigation.

THE BIOCHEMICAL LABORATORY, CAMBRIDGE. [*Received, December 9th*, 1940.]

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30. *Catalytic Toxicity and Chemical Structure. Part VII. Elimination of Catalyst Poisons by Conversion into Derivatives of Shielded Type.*

By EDWARD B. MAXTED and ROBERT W. D. MORRISH.

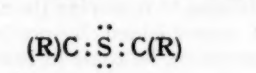
The conversion of catalyst poisons into non-poisonous derivatives of shielded type—in which the inherently poisonous element, by virtue of its possession of a stable saturated electron octet (see Part V), loses its characteristic toxic properties—

constitutes a method of eliminating catalyst poisons from impure systems which may be used as an alternative process to the often difficult actual removal of small traces of a poison by absorption or other means. The present paper contains a description of preliminary work dealing with the conversion, *in situ*, of poisons of sulphide type into non-toxic sulphones. The method has also been tried for thiophen, following preliminary hydrogenation with the object of forming tetrahydrothiophen, which, unlike the original thiophen, forms a sulphone on oxidation. A very substantial degree of detoxication was obtained in each case.

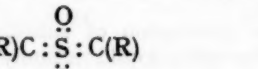
In Part V (J., 1940, 252) it was pointed out that, in general, the catalytically poisonous character of sulphur, selenium, tellurium, and phosphorus compounds towards metallic hydrogenation catalysts is dependent on the possession by the normally toxic element of unshared electron pairs. Accordingly—save in certain phosphorus compounds, in which cases of relatively weak bond strengths between phosphorus and hydrogen occur—catalytic toxicity was found to disappear if the compound containing the inherently poisonous element has a structure in which this element is shielded by the possession of a completely shared electron octet which is stable under the conditions employed for catalysis. For instance, the hydrides of these elements, such as hydrogen sulphide or phosphine, and the sulphides, thiols, sulphites, selenites, tellurites, thiosulphates, tetrathionates, and the free elements themselves, where these are sufficiently soluble, are toxic towards platinum, whereas sulphates, sulphonates, selenates, tellurates, and phosphates are non-toxic. It should be noted, however, that, in the case of compounds of certain other characteristically poisonous elements, *e.g.*, arsenic or antimony, the necessary stability of structure of the compound during subsequent catalysis is usually absent, in that most arsenic or antimony compounds become hydrogenated to toxic arsine or stibine; and, for this reason, this shielding effect is not in general effective with arsenic or antimony, at any rate as far as their toxicity in catalytic hydrogenation is concerned.

Since the removal of small traces of catalyst poisons from impure substances prior to their hydrogenation is often difficult, particularly if the poisons are in a relatively inert or not easily absorbable form such as an organic sulphide or thiophen, it seemed possible that the above principle could be utilised as the basis of a method for eliminating poisons, the process involved being the conversion of the poison into a shielded non-toxic derivative rather than its actual removal.

In the case of organic sulphides, a convenient shielded derivative appeared to be the sulphone (II), which, unlike the original sulphide (I), possesses a saturated electronic structure. Cyclic sulphides of the thiophen type, however, cannot be oxidised directly



(I.) Sulphide (toxic).



(II.) Sulphone (non-toxic).

to a sulphone; but, since tetrahydrothiophen readily forms a sulphone, a possible method of dealing with cyclic poisons of the thiophen class, including substances such as thionaphthen, which occur as poisons in commercial benzene and naphthalene, seemed to be by way of the hydrogenated derivative, followed by the conversion of this into the sulphone.

Further, the conversion of a poison into a sulphone is obviously only one of many possible methods for the elimination of the unsaturated electron pairs which are apparently necessary for the formation of the relatively strong chemisorptive linkage between the poisonous atom and the catalyst which underlies the toxic action; and the effectiveness of any particular method will depend on the degree of completeness of the conversion obtainable under the experimental conditions used.

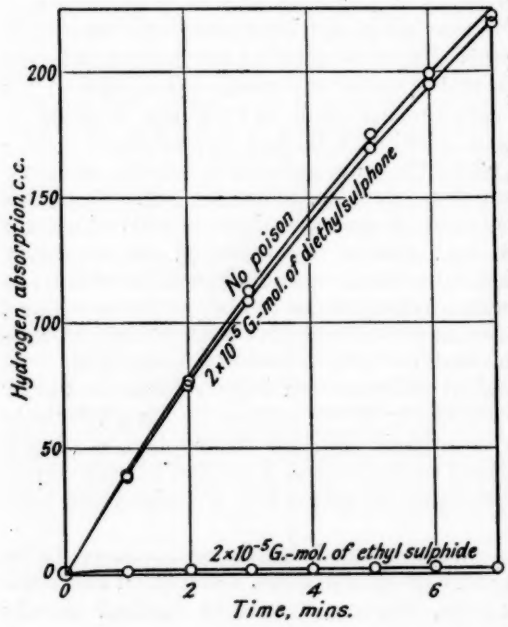
Experimental.

In the present work, platinum was used as the catalyst throughout, and the technique employed for measuring its activity for catalytic hydrogenation in the presence of a known quantity of the poison, or of its shielded derivative, was similar to that adopted in previous papers of this series (J., 1937, 603, 1004; 1938, 455, 839; 1940, 252, 469). Crotonic acid was,

as before, employed as a convenient standard ethylenic substance for hydrogenation; and, in general, the system taken for each activity measurement consisted of 5 c.c. of a 2N-solution of crotonic acid in acetic acid, 0·05 g. of stock platinum-black, and a further 5 c.c. of acetic acid containing the poison or its derivative. In those runs in which the conversion of the poison into its shielded derivative was carried out *in situ*, *viz.*, in all runs after those grouped together in Fig. 1, 1 c.c. of water, containing the reagent used for the conversion, was substituted for 1 c.c. of the acetic acid, since this reagent was more conveniently added in aqueous solution; and, in all cases, the blank runs, *viz.*, the measurements of the activity of the catalyst in the absence of the poison or its derivative, were of course made in a solvent of the same composition as that used with the poison. The hydrogenation was carried out in a shaker, at 25°.

Detoxication of Ethyl Sulphide.—In order, first of all, to obtain a quantitative comparison of the toxic effect exerted by ethyl sulphide before and after complete conversion into sulphone, a specimen of this sulphide was oxidised to diethylsulphone, sodium hypochlorite being used as the oxidising agent (Wood and Travis, *J. Amer. Chem. Soc.*, 1928, **50**, 1226); and, in this case only, the sulphone was isolated as such and purified by recrystallisation from alcohol.

Fig. 1.



The general effect of approximately equal quantities (about 2×10^{-5} g.-mol.) of the sulphide and of the sulphone on the activity of 0·05 g. of the platinum catalyst is shown in Fig. 1, from which it will be seen that, whereas the activity of the catalyst is almost completely suppressed by the sulphide, the same weight of sulphur in the form of the sulphone has substantially no toxic action. In the sulphide curve, the very small hydrogen absorption, which occurred mainly in the first minute, is probably largely due to solution.

The next step consisted in examining the extent to which small quantities of ethyl sulphide, contained as a poison in a hydrogenation system, can be eliminated *in situ*, without isolating either the sulphide or the sulphone into which it is converted. In order to produce the effect of a complete removal of the poison, the conditions chosen for the oxidation should, in addition to removing the sulphide itself, also avoid the production of substantial quantities of non-shielded by-products such as the sulphoxide, which would not only, by reason of its structure, be toxic in itself but would also, unlike the sulphone, be reduced back to sulphide during subsequent hydrogenation.

The result of treating the poison *in situ* with sodium hypochlorite is shown in Fig. 2, in which Curve I represents the rate of hydrogenation of the standard quantity of crotonic acid containing $1{\cdot}85 \times 10^{-6}$ g.-mol. of ethyl sulphide, Curve II a similar charge with the addition of 1×10^{-3} g.-mol. of sodium hypochlorite, and Curve III is a blank run consisting of crotonic acid alone without any poison. It will be seen that the toxic effect of the sulphide substantially disappears.

It was considered of interest to investigate in somewhat greater detail the influence of the quantity of hypochlorite on the degree of effective elimination of the poison, particularly since the amount used in the series summarised in Fig. 2, although small in actual amount, represents a large excess (about 250 times) over that required for the oxidation of the very small quantity of poison present. To this end a series of runs was carried out in which various quantities of hypochlorite were added to a standard hydrogenation system containing, as before, $1{\cdot}85 \times 10^{-6}$ g.-mol. of ethyl sulphide, 5 c.c. of 2N-crotonic acid in acetic acid, 1 c.c. of water, and 0·05 g. of platinum, the hypochlorite being in each case added with the 1 c.c. of water. The mixture was allowed to remain for about 10 mins. in air in the hydrogenation pipette before the air was replaced by hydrogen. The reaction course followed during the subsequent hydrogenation was, as is usual, very nearly linear up to an advanced stage of hydrogenation; and the hydrogenation rates could accordingly be conveniently compared by taking the average hydrogen absorption per min. for the first 5 mins. after the initial minute—

this was excluded since uniform shaking conditions (including the uniform distribution of the finely divided catalyst throughout the liquid system) are in most cases not attained until some 15—30 secs. after starting the shaker. As an example of the degree of variation of the rate in a given run during the 5 mins. over which the average was taken, the actual hydrogen absorption per min., in a run with $1{\cdot}22 \times 10^{-4}$ g.-mol. of hypochlorite, was 13·0, 13·4, 13·6, 13·7, and 13·4 c.c., respectively, during the second, third, fourth, fifth, and sixth minutes of the run, giving an average velocity of 13·4 c.c./min. The extent of the detoxication obtained

FIG. 2.

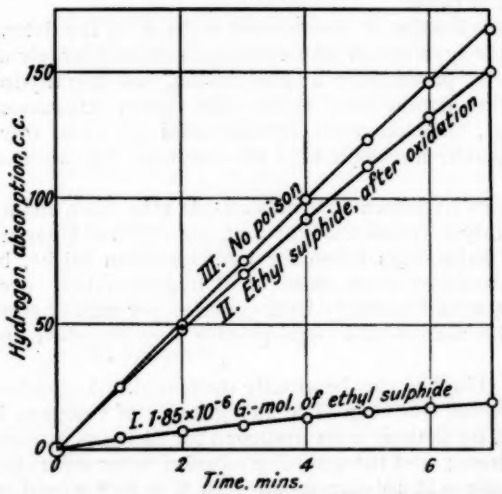
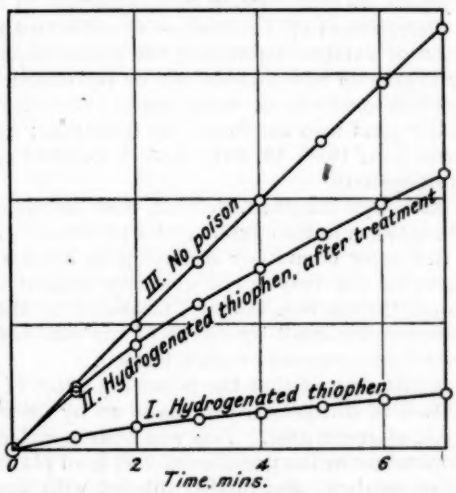


FIG. 3.



with various quantities of hypochlorite is shown in the table. The fractional activities in the last column represent the activity of the catalyst expressed as a fraction of its unpoisoned activity, and are accordingly a measure of the effective elimination of the poison. The concentration of the ethyl sulphide was $1{\cdot}85 \times 10^{-6}$ g.-mol. throughout.

G.-mols. of NaOCl added, $\times 10^6$.	Hydrogenation velocity, c.c./min.	Fractional activity of catalyst.	G.-mols. of NaOCl added, $\times 10^6$.	Hydrogenation velocity, c.c./min.	Fractional activity of catalyst.
0	2·4	0·099	32·4	17·0	0·70
1·1	3·1	0·128	57·5	19·3	0·80
2·2	5·0	0·206	85·6	20·6	0·85
4·65	8·9	0·366	120	22·7	0·93
12·2	13·4	0·55	Unpoisoned velocity	24·3	1·00

It will be seen that the degree of restoration of the activity of the catalyst increases progressively with the amount of oxidising agent introduced and that, at any rate with the higher concentrations of hypochlorite, substantially complete suppression of the toxic action of the ethyl sulphide can be obtained.

For the strict assessment of the degree of detoxication, however, two possible small corrections have to be considered. First, the unchanged hypochlorite present may itself undergo catalytic hydrogenation and thus absorb hydrogen during the run, with consequent influence both on the apparent speed of hydrogenation and on the total hydrogen absorbable. Secondly, the presence of hypochlorite may affect the hydrogenation rate by changing the viscosity of the solution.

These points were investigated by blank runs with hypochlorite, crotonic acid, and platinum in the absence of the poison. The possible additional absorption of hydrogen by quantities of hypochlorite of the order used is in any case small compared with the total hydrogen absorbed during the runs. Its volume varies from 0·25 c.c. for the run with $1{\cdot}1 \times 10^{-5}$ g.-mol. to 23 c.c. for the run with 1×10^{-3} g.-mol. of hypochlorite, compared with an uncorrected volume of over 230 c.c. absorbed by the crotonic acid. As an example of the total absorption observed, the reaction in the run with $8{\cdot}6 \times 10^{-4}$ g.-mol. of hypochlorite came, after 10 mins., to the relatively abrupt halt characteristic of these hydrogenation processes, 239 c.c. of hydrogen being absorbed. This is almost exactly the calculated value, at the temperature and pressure of the run, for the crotonic acid present: accordingly, only a negligible additional volume was absorbed by the hypochlorite, the calculated possible absorption by this being in any case only about 20 c.c.

The effect of hypochlorite, in the absence of poison, on the velocity of hydrogenation (as distinct from its effect on the total hydrogen required for saturation) was tested similarly. In a series of six blank runs with from 1×10^{-5} to about 1×10^{-3} g.-mol. of hypochlorite, which covers the range used in the above table, the hydrogenation velocity was found to vary somewhat irregularly, the mean velocity being 24·0 c.c./min. (cf. 24·3 c.c. in table) and the maximum variation either way being about 10%. It is probable that the above relatively small variation is caused by chance differences in the hypochlorite solutions (which have to be prepared fresh for each run), but in any case the correction was too small and too irregular to justify its introduction as a correction in the table.

Detoxication of Thiophen.—The effective application of the present method to the detoxication of catalyst poisons of the cyclic sulphur type would be expected to depend largely on the degree to which these can be converted, by preliminary hydrogenation, into tetrahydrothiophen derivatives, since these reduced ring compounds, unlike the parent substances, readily pass into sulphones on oxidation; *e.g.*, Grischkevitsch-Trochimovski (*J. Russ. Phys. Chem. Soc.*, 1916, **48**, 901) readily oxidised tetrahydrothiophen to the sulphone by means of permanganate.

Although thiophen, in bulk, does not absorb hydrogen at a measurable rate when shaken with this gas in the presence of a platinum catalyst, it was thought that quantities of thiophen of the order commonly occurring in impure substances taken for hydrogenation might, by reason of the very small quantity present, undergo some measure of hydrogenation, even though the reaction velocity, measured by the actual quantity hydrogenated per unit of time, is necessarily small by virtue of the still toxic nature (and consequently long adsorbed life) of the hydrogenated product formed.

Trials showed that the poisoning effect of thiophen can be greatly decreased. A standard solution of this poison was made up by dissolving 0·0084 g. (1×10^{-4} g.-mol.) of thiophen in 10 c.c. of acetic acid. This was hydrogenated by shaking with hydrogen for 3½ hours at room temperature in the presence of 0·05 g. of platinum; and the resulting solution, after separation of the catalyst, was further diluted with acetic acid to correspond with 2×10^{-6} g.-mol. of poison per c.c. This concentration is approximate only, since some of the thiophen is undoubtedly adsorbed by the platinum used for the hydrogenation; but the hydrogenated solution was, like the original thiophen, strongly toxic: *e.g.*, 1 c.c. of the hydrogenated solution, when added to a normal hydrogenation charge containing 5 c.c. of 2N-crotonic acid and 0·05 g. of platinum (together with the usual additional acetic acid and water), reduced the hydrogenation rate to about 2·5 c.c./min. (Curve I, Fig. 3) compared with an unpoisoned rate of about 25 c.c./min. (Curve III). In order to test the degree of detoxication obtained by treating this type of poison, *in situ*, with hypochlorite, a parallel hydrogenation run was now made with a similar system containing $8{\cdot}5 \times 10^{-4}$ g.-mol. of hypochlorite in addition to the hydrogenated thiophen. The detoxication was, as with the runs with ethyl sulphide, carried out in the presence of the crotonic acid and of the platinum; and it was found advantageous to allow the oxidising agent to remain in contact with the poison for at least 20 mins., the whole system being shaken, in the presence of air, in the hydrogenation pipette before displacing the air with hydrogen and proceeding to hydrogenation. The improvement obtained is shown by the results plotted in Curve II. It will be seen that, although complete detoxication was not attained under the conditions used, the hydrogenation rate was raised from about 2·5 c.c. to about 15 c.c. per min. by the oxidising treatment; and this rise was confirmed by a duplicate run. However, with these cyclic sulphur compounds, the conversion into a sulphone depends on a two-stage process, and, with the small quantity of thiophen used in making up the standard poisoning solution, it was difficult to assess accurately the amount of hydrogenation actually obtained in the first stage (the conversion of thiophen into tetrahydrothiophen), since the total volume of hydrogen absorbable by 1×10^{-4} g.-mol. of thiophen is only of the order of 4 c.c. The effective degree of detoxication by the complete treatment corresponded with an approximately 60% restoration of the unpoisoned reaction rate, compared with an approximately 85% restoration obtained with ethyl sulphide with the same quantity of hypochlorite. Further, in view of the technical importance of thiophen as a catalyst poison, the above work—which at any rate indicates a possible method for its elimination—is necessarily only of a preliminary nature. In particular, the effectiveness of other means of oxidation, including anodic oxidation, on all these types of sulphur poisons remains to be tried.

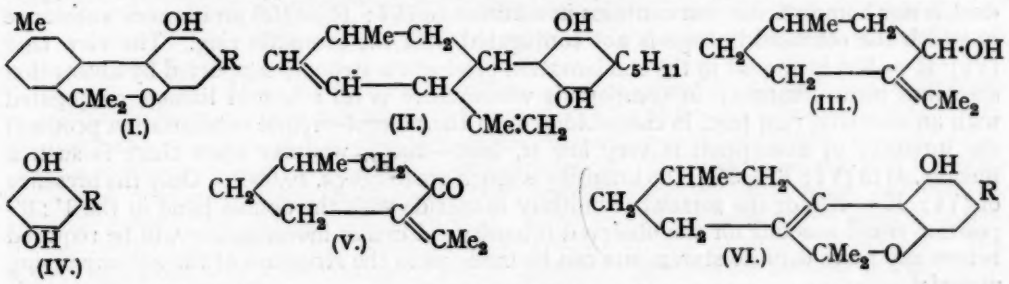
UNIVERSITY OF BRISTOL. [*Received, November 5th*, 1940.]

31. Cannabis Indica. *Part VI. The Condensation of Pulegone with Alkyl Resorcinols. A New Synthesis of Cannabinol and of a Product with Hashish Activity.*

By R. Ghosh, A. R. Todd, and D. C. Wright.

The condensation of terpene derivatives with orcinol and olivetol has been studied in connection with suggestions made as to the biogenesis of certain constituents of *Cannabis* resins (Part II, Jacob and Todd, J., 1940, 649). Crude pulegol, prepared by reduction of pulegone, when heated with orcinol in presence of zinc chloride, yielded, as expected, a hexahydrodibenzopyran derivative. Pulegone itself condensed with orcinol in presence of formic acid to give a product which appeared to be a mixture of isomerides, including (VI; R = Me); dehydrogenation of the product yielded *6″-hydroxy-2 : 2 : 5′ : 4″-tetramethyldibenzopyran* (I; R = Me), identified by comparison of its p-*nitrobenzoate* with that of a specimen prepared by dehydrogenating (VI; R = Me). Pulegone and olivetol condensed similarly to give a product with the composition of a tetrahydrocannabinol. This product had about half the hashish activity shown by a pure specimen of the tetrahydrocannabinol (VI; R = C_5H_{11}) (Gayer test) and is probably a mixture of this substance with some isomeride in which the ethenoid linkage is not conjugated with the aromatic ring. Dehydrogenation of the pulegone–olivetol condensation product yielded cannabinol, identified as its *p*-nitrobenzoate.

Of the substances hitherto isolated from *Cannabis* resin, cannabinol has been shown by synthesis to be 6″-hydroxy-2 : 2 : 5′-trimethyl-4″-*n*-amyldibenzopyran (I; R = C_5H_{11}) (Adams, Baker, and Wearn, *J. Amer. Chem. Soc.*, 1940, **62**, 2204; Ghosh, Todd, and Wilkinson, Parts IV and V, J., 1940, 1121, 1393), and cannabidiol is believed to have structure (II), in which the position of the cyclic ethylenic linkage has not been rigidly established (Adams, Loewe, Pease, Cain, Wearn, Baker, and Wolff, *J. Amer. Chem. Soc.*, 1940, **62**, 2566). It has been suggested (Part II; *loc. cit.*) that these compounds might arise in the plant by condensation of a terpene derivative with olivetol. The initial product of such a condensation might be cannabidiol, from which, by cyclisation, a tetrahydrocannabinol could be produced; dehydrogenation of the cyclised material would give cannabinol. It has been shown by Adams, Pease, Cain, and Clark (*J. Amer. Chem. Soc.*, 1940, **62**, 2402) that cannabidiol can be cyclised, yielding, according to conditions, one or more tetrahydrocannabinols which exhibit the characteristic pharmacological properties of the hemp drugs when tested on dogs. As these products can be dehydrogenated to cannabinol, it is clear that part, at any rate, of this hypothetical scheme of biogenesis is capable of realisation in the laboratory. The observation is of added interest since it seems probable that the activity of the hemp drugs may be due, in part at least, to the presence in them of one or more tetrahydrocannabinols. For some time we have been studying the possibility of synthesising cannabinol by direct condensation of terpene derivatives with olivetol, followed by dehydrogenation. Such a synthetic process would be attractive not merely in connection with the above scheme but also because the inter-



mediate, partially hydrogenated cannabinols formed in the synthesis might, if an optically active terpene derivative were used, themselves be at once optically and pharmacologically

active like the cyclised isomerides of cannabidiol. The fact that the synthesis of cannabinol has been achieved in this way warrants the publication of our results at this stage.

In the vitamin E group α-tocopherol has been synthesised by several methods, including the condensation of phytol with ψ-cumoquinol (Bergel, Copping, Jacob, Todd, and Work, J., 1938, 1382). By analogy it was to be expected that pulegol (III) would condense with olivetol (IV; R = C_5H_{11}) to give a hexahydrocannabinol. The preparation of pulegol from pulegone by reduction with aluminium *iso*propoxide has been described by Doeuvre and Perret (*Bull. Soc. chim.*, 1935, **2**, 298), who record rather poor yields. In our hands the method of these authors gave rise to a mixture containing in addition to pulegol a considerable proportion of doubly unsaturated compounds, since it showed selective light absorption in the neighbourhood of 2350 A. No better results were achieved by reduction of pulegone with aluminium *iso*propoxide in *iso*butyl alcohol, following the procedure used by Malcolm and Read (J., 1939, 1037) for the reduction of Δ^4-menthen-3-one. When the crude pulegol obtained by either of these methods was heated in decalin solution with orcinol (IV; R = Me) in presence of anhydrous zinc chloride, condensation occurred and a thick, yellowish, alkali-insoluble oil was produced, which distilled at a fairly constant temperature and appeared from analysis and properties to consist essentially of the expected *6″-hydroxy-2 : 2 : 5′ : 4″-tetramethyl-1′ : 2′ : 3′ : 4′ : 5′ : 6′-hexahydrodibenzopyran.* The condensation was, however, unsatisfactory in so far as one of the starting materials was of doubtful composition, and attention was directed to the condensation of the readily accessible pulegone (V) with resorcinol derivatives. As far as we are aware the condensation of αβ-unsaturated ketones with phenols to produce chromens has not been hitherto reported, but by analogy with the well-known Doebner–v. Miller synthesis of quinoline derivatives it might be expected that the condensation of (V) with (IV) would yield a tetrahydrodibenzopyran derivative (VI). It was indeed observed that, on heating pulegone with orcinol in presence of formic acid (98—99%) and subsequently hydrolysing the product to remove any formyl groups introduced, a thick alkali-insoluble oil was obtained, which distilled at a more or less constant temperature and was then colourless; several samples were analysed and had the composition of the expected product (VI; R = Me). That this material had the tetrahydrodibenzopyran structure was demonstrated by dehydrogenation with palladised charcoal; 2 mols. of hydrogen were evolved and *6″-hydroxy-2 : 2 : 5′ : 4″-tetramethyldibenzopyran* (I; R = Me) was produced. The identity of this product was established by comparison of its p-*nitrobenzoate* with the corresponding ester of the product obtained by dehydrogenating authentic 6″-hydroxy-2 : 2 : 5′ : 4″-tetramethyl-3′ : 4′ : 5′ : 6′-tetrahydrodibenzopyran (VI; R = Me) (Part IV; *loc. cit.*).

The products from different pulegone–orcinol condensations showed absorption spectra closely similar to one another and to that of (VI; R = Me) as regards the position of the maximum, but the intensity of light absorption varied. In general the intensity was only about half that shown by a pure specimen of (VI; R = Me), although in one case a fraction was obtained showing an intensity of a similar order. Moreover (VI; R = Me) is a crystalline solid (Part IV, *loc. cit.*; Adams, Pease, Cain, Clark, Wolff, and Wearn, *J. Amer. Chem. Soc.*, 1940, **62**, 2245), and in no case could the pulegone–orcinol products be crystallised. The most probable explanation of these facts is that the condensation product is not homogeneous but contains in addition to (VI; R = Me) an isomeric substance in which the ethenoid linkage is not conjugated with the aromatic ring. The view that (VI; R = Me) is present in the condensation products is strongly supported by absorption spectrum measurements; in compounds where there is no ethenoid linkage conjugated with an aromatic ring (*e.g.*, in cannabidiol or in the pulegol–orcinol condensation product) the intensity of absorption is very low (ε, 1000—2000), whereas when there is such a linkage, as in (VI; R = Me), the intensity is much greater (ε *ca.* 10,000). Only the presence of (VI; R = Me) or the somewhat unlikely isomeride with the double bond in the 1′ : 6′-position could account for the observed intensity. Further investigation will be required before any more definite statements can be made as to the structure of the accompanying material.

Olivetol (IV; R = C_5H_{11}) underwent condensation with pulegone in presence of formic acid under conditions similar to those used in the case of orcinol. The product, a slightly

yellowish oil, had the composition of a tetrahydrocannabinol. In accordance with such a structure the oil, on being heated to 300° with palladised charcoal, evolved 2 mols. of hydrogen and gave a colourless resin with the composition and reactions of cannabinol (I; $R = C_5H_{11}$); the product was identified by conversion into its crystalline *p*-nitrobenzoate, whose m. p. was undepressed on admixture with authentic cannabinol *p*-nitrobenzoate. It may be mentioned in passing that, although cannabinol has been obtained in crystalline form by Adams and his collaborators, no specimen, synthetic or natural, has so far crystallised in our laboratories; there is, however, no doubt as to the identity of the materials handled by both groups of workers, since they give derivatives with identical properties. The pulegone–olivetol condensation product resembled the pulegone–orcinol product in that its absorption spectrum showed a single band similar to but only about half as intense as that shown by the tetrahydrocannabinol (VI; $R = C_5H_{11}$); similar views are held regarding its composition.

In Part IV (*loc. cit.*) the synthesis of (VI; $R = C_5H_{11}$) was described and it was mentioned that pharmacological investigations on it were then incomplete. The results of tests by Prof. A. D. Macdonald have shown that the substance exhibits hashish activity in the Gayer test on rabbits at a dose of 1 mg./kg.; it has thus activity similar in degree to that of a distilled Indian hemp resin. Details of the pharmacological examination of this and other synthetic substances will be reported elsewhere. The activity of the same compound in dogs has been reported in the interim by Adams, Loewe, Pease, Cain, Wearn, Baker, and Wolff (*loc. cit.*). The pulegone–olivetol condensation product, which had little or no optical activity, was pharmacologically active in the Gayer test at a dose of 2·5 mg./kg. and inactive at 1 mg./kg., *i.e.*, it had about half the activity of a pure specimen of (VI; $R = C_5H_{11}$). Since the spectroscopic evidence suggests that only about half of the product is (VI; $R = C_5H_{11}$), it would appear that the remainder has little or no hashish activity.

It is clear that the procedure above described opens up a new route to the synthesis of substances which may show hashish activity. The synthetic method also affords some support for the hypothetical scheme suggested for the biogenesis of *Cannabis* constituents; in this connexion a knowledge of the composition of the terpene fraction obtained in the distillation of hemp resin would be of the greatest interest.

Experimental.

Condensation of Pulegol with Orcinol.—Crude pulegol (20 g.), obtained from pulegone by the method of Doeuvre and Perret (*loc. cit.*), orcinol monohydrate (10 g.), powdered anhydrous zinc chloride (20 g.), and decalin (200 c.c.) were heated together at 130—140° during 2 hours. After cooling, the decalin solution was decanted, diluted with ether, washed several times with aqueous sodium hydroxide (10%), dried, and evaporated, first under atmospheric pressure, then in a vacuum to remove decalin and unchanged pulegol. The residue distilled fairly steadily at 140—150° (bath temp.)/10^{-2} mm., very little material boiling outside this range. The product, a yellowish viscous oil, gave a blue colour with 2 : 6-dichlorobenzoquinonechloroimide, and from its analysis appeared to be the expected *6″-hydroxy-2 : 2 : 5′ : 4″-tetramethyl-1′ : 2′ : 3′ : 4′ : 5′ : 6′-hexahydrodibenzopyran* [Found: C, 79·2, 79·2; H, 9·6, 9·5; active H (Zerewitinoff), 0·40. $C_{17}H_{24}O_2$ requires C, 78·5; H, 9·3; 1 active H, 0·38%]. *Light absorption in alcohol:* Max. 2800 A. (ε 1300); min. 2670 A. It gave no coloration with alcoholic potassium hydroxide.

Condensation of Pulegone with Orcinol.—A mixture of pulegone (5 c.c.), orcinol monohydrate (5·5 g.), and formic acid (30 c.c. of 98—99%) was refluxed for 3½ hours. The resulting brownish solution was evaporated on the water-bath under reduced pressure, the residue made alkaline, and the excess of pulegone removed by steam-distillation. The viscous oil obtained from the distillation residue by ether extraction was hydrolysed by refluxing for 1½ hours with methyl-alcoholic potassium hydroxide (25 c.c. of 4%). After removal of most of the methyl alcohol by distillation the mixture was cooled, diluted with water, and extracted with ether. The extract was dried over sodium sulphate and evaporated; the residue distilled at 150° (bath temp.)/2 × 10^{-3} mm. as a colourless viscous oil which could not be crystallised (Found: C, 78·9; H, 8·8. $C_{17}H_{22}O_2$ requires C, 79·1; H, 8·5%). *Light absorption in alcohol:* Max. *ca.* 2750 A. (ε *ca.* 5000); min. 2500 A. There was no evidence of separation into distinct fractions

by distillation or chromatographic analysis; arbitrarily selected fractions all had the same composition and differed but little in intensity of light absorption. In one instance, however, a product was obtained showing a maximum at 2770 A. of intensity ε 9620 (Found: C, 78·8; H, 9·0%) [(VI; R = Me) has max. 2790 A. (ε 10,980); min. 2500 A.]. The condensation products obtained in all the experiments gave a blue colour with 2 : 6-dichlorobenzoquinonechloroimide but gave no coloration with alcoholic potassium hydroxide.

6″-Hydroxy-2 : 2 : 5′ : 4″-tetramethyldibenzopyran (I; R = Me) (This experiment was carried out by Mr. P. B. Russell, B.Sc., to whom our thanks are due).—6″-Acetoxy-2 : 2 : 5′ : 4″-tetramethyl-3′ : 4′ : 5′ : 6′-tetrahydrodibenzopyran (VI; R = Me) (0·5 g.) (Part IV, *loc. cit.*) was heated with palladised charcoal (0·2 g.) at 300—320° until evolution of hydrogen ceased (hydrogen evolved, 73 c.c. Calc. for $2H_2$, 75 c.c.). The product was extracted from the charcoal with ether, the acetyl group removed by hydrolysis with methyl-alcoholic potassium hydroxide, and the *dibenzopyran* (I; R = Me) distilled at 152° (bath temp.)/10^{-3} mm. It was obtained as a colourless viscous oil which showed a tendency to crystallise on long standing (Found: C, 79·8; H, 7·2. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%). *Light absorption in alcohol:* Max. 2820 A. (ε 14,740); min. 2500 A. On refluxing in pyridine solution with *p*-nitrobenzoyl chloride a p-*nitrobenzoate* was obtained, which crystallised from alcohol in pale yellow needles, m. p. 215—216° (Found: N, 3·7. $C_{24}H_{21}O_5N$ requires N, 3·5%).

Dehydrogenation of the Pulegone–Orcinol Condensation Product.—The distilled condensation product (0·23 g.) was heated with palladised charcoal (0·11 g.) at 300—320° for *ca.* 1 hour until evolution of hydrogen ceased (hydrogen evolved, 39 c.c. Calc. for $2H_2$, 40 c.c.). The product was extracted from the charcoal with ether and distilled, coming over as a colourless viscous oil at 150—160° (bath temp.)/10^{-3} mm. (Found: C, 80·0; H, 7·3. Calc. for $C_{17}H_{18}O_2$: C, 80·3; H, 7·1%). In accordance with experience of analogous cases (cf. Part V; *loc. cit.*) it was observed that the dehydrogenation proceeded more smoothly and rapidly when the acetate of the pulegone–orcinol condensation product was employed. The identity of the dehydrogenation product with 6″-hydroxy-2 : 2 : 5′ : 4″-tetramethyldibenzopyran was confirmed by preparation of its *p*-nitrobenzoate, which crystallised from alcohol in pale yellow needles, m. p. 215—216°, undepressed by the specimen described above.

Condensation of Pulegone with Olivetol.—Pulegone (1·5 c.c.), olivetol monohydrate (1 g.), and formic acid (7 c.c. of 98—99%) were refluxed for 3 hours, and the product isolated as before. The colourless viscous oil obtained distilled at 170° (bath temp.)/10^{-3} mm. [Found: C, 80·3; H, 9·5; active H (Zerewitinoff), 0·31. $C_{21}H_{30}O_2$ requires C, 80·3; H, 9·6; 1 active H, 0·31%]. *Light absorption in alcohol:* Max. 2760 A. (ε, 6200); min. 2500 A. [(VI; R = C_5H_{11}) has max. 2755 A. (ε, 11,130); min. 2490 A.]. The material gave a blue colour with 2 : 6-dichlorobenzoquinonechloroimide but gave no coloration with alcoholic potassium hydroxide. It appeared to have an insignificant lævorotation in acetone solution and was pharmacologically active in the Gayer test on rabbits.

Dehydrogenation of the Pulegone–Olivetol Condensation Product to Cannabinol.—The condensation product (0·37 g.) was dehydrogenated by heating at 300—320° with palladised charcoal (0·2 g.) in the usual manner (hydrogen evolved, 51 c.c. Calc. for $2H_2$, 53 c.c.). The product, which distilled as a slightly yellowish resin at 160—170° (bath temp.)/10^{-2} mm., showed the colour reactions of cannabinol. It was identified by heating with *p*-nitrobenzoyl chloride in pyridine solution, giving a *p*-nitrobenzoate, m. p. 160—162°, undepressed by authentic cannabinol *p*-nitrobenzoate (m. p. 162—163°).

Grateful acknowledgment is made to the University of Calcutta for a Sir T. N. Palit foreign research scholarship held by one of us (R. G.) and to Messrs. Roche Products, Ltd., for a grant.

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32. *Application of the Diene Synthesis to Terpenoid Compounds. Part II. Observations on the Esters derived from some Maleic Anhydride Adducts.*

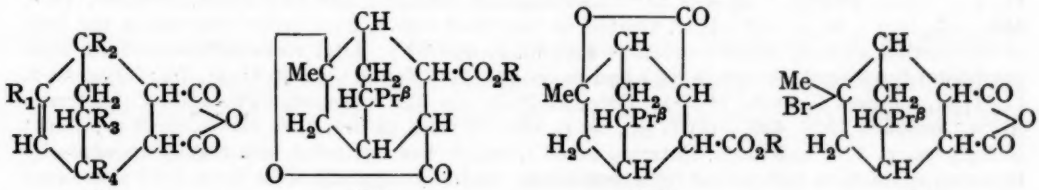
By T. F. WEST.

In Part I (J., 1940, 1162) it was found that the eucarvone–maleic anhydride adduct, like the caryophyllene adduct, gives dialkyl esters with alcoholic solutions of hydrogen chloride. It is now shown that the maleic anhydride adducts derived from $\Delta^{1:3}$-*cyclo-*

hexadiene, myrcene, and anthracene behave similarly, whereas the *cyclo*pentadiene adduct, like that from α-phellandrene, gives a monoalkyl lactonic ester. The reaction lends support to the suggestion of Goodway and West (J., 1940, 702) that the α-terpinene–maleic anhydride adduct is derived from a mixture of terpenes. The colour reactions of a number of terpenoid compounds with a solution of tetranitromethane are described.

GOODWAY and WEST (J., 1939, 1853) have drawn attention to the fact that, although the maleic anhydride adducts from α-phellandrene and di*cyclo*hexenyl yield monoalkyl lactonic esters with alcoholic solutions of hydrogen chloride, the caryophyllene adduct, considered by Rydon (J., 1939, 537) to be derived from a conjugated *cyclo*heptadiene, gives dialkyl esters. On the other hand, West (J., 1940, 1162) has obtained dialkyl esters from the eucarvone–maleic anhydride adduct with both methyl- and ethyl-alcoholic hydrogen chloride.

It has now been found that similar treatment of the α-terpinene–maleic anhydride adduct with methyl-alcoholic hydrogen chloride leads to a mixed product, whereas the $\Delta^{1:3}$-*cyclo*hexadiene–maleic anhydride adduct gives a dialkyl ester exclusively and in good yield. The formulæ assigned by Diels and his co-workers being accepted, it is remarkable that these substituted *bicyclo*[2 : 2 : 2]octane systems derived from $\Delta^{1:3}$-*cyclo*hexadiene (I; R_1, R_2, R_3 and R_4 = H), α-phellandrene (I; R_1 = Me, R_3 = Pr^β, R_2 and R_4 = H), and α-terpinene (I; R_2 = Me, R_4 = Pr^β, R_1 and R_3 = H) behave differently. The result lends support to the inference of Goodway and West (J., 1940, 702) that the α-terpinene adduct may be an impure product derived from a mixture of terpenes in which α-terpinene predominates (cf. Booker, Evans, and Gillam, J., 1940, 1463). Furthermore, considered with the ease of addition of maleic anhydride to eucarvone (West, *loc. cit.*), it may be significant that Alder and Rickert (*Ber.*, 1937, **70**, 1364) obtained evidence, from an examination of the condensation products formed with acetylenedicarboxylic ester, for the presence of 1 : 5 : 5-trimethyl-$\Delta^{1:3}$-*cyclo*heptadiene in the α-terpinene prepared in the usual manner by the dehydration of α-terpineol. Hultzsch (*Ber.*, 1939, **72**, 1173) has reported that the α-phellandrene–maleic anhydride adduct cannot be reduced and that the corresponding dicarboxylic acid is unobtainable. The cause of the variation is not obvious from an examination of models and the reason for the formation of *dimethyl* esters from the maleic anhydride adducts derived from myrcene, isoprene, and anthracene and a *monomethyl lactonic* ester from the *cyclo*pentadiene adduct is equally obscure.



(I.) (II.) (III.) (IV.)

The conclusions of Linstead and Rydon (J., 1933, 580) and Adams and Gruber (*J. Amer. Chem. Soc.*, 1938, **60**, 2792) being applied, the formulæ (II) and (III) are the most probable for the lactonic esters * obtained from the α-phellandrene–maleic anhydride adduct. In an attempt to confirm this conclusion the methyl ester was treated with a solution of hydrogen bromide, followed by acetyl chloride. In analogy with the results of Koch (Dissert., Kiel, 1932) the formation of the bromo-anhydride (IV) was expected, but in practice the only product isolated was a monobasic *lactonic* acid identical with the acid (II) or (III) (R = H) obtained by saponifying the methyl ester.

A solution of tetranitromethane produces a yellow colour with the dimethyl esters

* (Joint note with Dr. N. F. Goodway.) In the paper of Goodway and West (J., 1938, 2028), page 2031, line 20 *et seq.* should read " 0·1378 G. of the methyl ester, dissolved in neutral alcohol by heating to 50°, required 0·3 ml. of 0·05N-sodium hydroxide ($C_{14}H_{21}O_2{\cdot}CO_2H$ requires 10·4 ml.). 0·115 G. of the ethyl ester under the same conditions required 0·5 ml. ($C_{15}H_{23}O_2{\cdot}CO_2H$ requires 8·2 ml.)."

obtained from the myrcene–, isoprene–, anthracene– and $\Delta^{1:3}$-*cyclo*hexadiene–maleic anhydride adducts and the product derived from the α-terpinene adduct. The monomethyl lactonic esters from the α-phellandrene and *cyclo*pentadiene adducts display no evidence of unsaturation. The eucarvone–maleic anhydride adduct finds another analogy with the caryophyllene adduct in not giving a reaction with tetranitromethane (cf. Ruzicka and Zimmermann, *Helv. Chim. Acta*, 1935, **18**, 219). On the contrary the dialkyl esters prepared from both these adducts (Goodway and West, J., 1939, *loc. cit.*; West, *loc. cit.*) show a yellow colour with the reagent. The presence of a double bond in the caryophyllene adduct remains uncertain (Ruzicka and Zimmermann, *loc. cit.*; Rydon, *loc. cit.*; Goodway and West, *loc. cit.*), but in the case of the eucarvone adduct the lack of evidence of unsaturation must reside in the non-reactive nature of the double bond observed in some polyterpenoid compounds (*Ann. Reports*, 1937, **34**, 328).

It is fortunate that the thoroughly investigated maleic anhydride adducts from *cyclo*pentadiene and $\Delta^{1:3}$-*cyclo*hexadiene provide, respectively, saturated mono- and unsaturated di-alkyl esters similar to those reported, in the present and previous papers, as derivable from terpenoid compounds. When circumstances permit, it is proposed to investigate further the constitution of the esters obtained from these typical adducts.

Experimental.

(Carbon and hydrogen determinations are by Drs. Weiler and Strauss, Oxford.)

Preparation of the Esters.—(*a*) The anthracene–maleic anhydride adduct (Clar, *Ber.*, 1931, **64**, 2198) (3 g.), m. p. 62°, was refluxed for 8 hours with 10 vols. of methyl alcohol saturated in the cold with dry hydrogen chloride. The crystals (2·9 g.) which separated on standing were recrystallised from methyl alcohol. The white *dimethyl* ester had m. p. 151° (Found: C, 74·4; H, 5·4; OMe, 18·85. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6; OMe, 19·25%). (*b*) Myrcene–maleic anhydride adduct (Diels and Alder, *Annalen*, 1928, **460**, 81) (10 g.), m. p. 34°, gave, on similar treatment and after removal of the alcohol, an oil which was kept for a few days over paraffin wax and solid caustic potash in a vacuum desiccator before purification by fractional distillation. The *dimethyl* ester (7·8 g.) had b. p. 176—178°/3 mm., $n_D^{20°}$ 1·4922 (Found: C, 68·5; H, 8·6; OMe, 21·9. $C_{16}H_{24}O_4$ requires C, 68·6; H, 8·6; OMe, 22·1%). (*c*) The isoprene–maleic anhydride adduct (Diels and Alder, *Annalen*, 1929, **470**, 101) (3·9 g.), m. p. 62—64°, treated as described in (*b*), gave a dimethyl ester which was not fully purified. It had b. p. 128—130°/3 mm. (Found: C, 60·3; H, 7·9; OMe, 23·1. $C_{11}H_{16}O_4$ requires C, 62·3; H, 7·5; OMe, 29·2%). (*d*) The $\Delta^{1:3}$-*cyclo*hexadiene adduct (Diels and Alder, *Annalen*, 1928, **460**, 115) (5 g.), m. p. 147—148°, treated as described above, gave, after removal of the bulk of the methyl alcohol, white crystals (4·4 g., m. p. 64—67°); after recrystallisation from light petroleum the *dimethyl* ester (3·2 g.) had m. p. 69—71° (Found: C, 64·5; H, 7·1; OMe, 28·2. $C_{12}H_{16}O_4$ requires C, 64·3; H, 7·1; OMe, 27·7%). (*e*) The *cyclo*pentadiene adduct (Diels and Alder, *Annalen*, 1928, **460**, 111) (7 g.), m. p. 164°, treated as described above, gave a product (6·5 g.) (m. p. 170° indefinite, sintering at 80°), which was separated into two components by repeated extraction with warm light petroleum. After recrystallisation from light petroleum the *monomethyl lactonic* ester (2·4 g.) had m. p. 83—84° (Found: C, 61·2; H, 6·0; OMe, 15·4. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·1; OMe, 15·8%). The monobasic *lactonic* acid, insoluble in light petroleum, crystallised from xylene in small blunt prisms (1·3 g.), m. p. 203—204° (Found: C, 59·5; H, 5·5; OMe, 0; equiv., 183. $C_9H_{10}O_4$ requires C, 59·3; H, 5·5%; equiv., 182). (*f*) In a typical experiment the α-terpinene–maleic anhydride adduct (Diels, Koch, and Frost, *Ber.*, 1938, **71**, 1163; cf. Goodway and West, J., 1940, 702) (7 g.), m. p. 62°, was refluxed for 8 hours with methyl-alcoholic hydrogen chloride (70 ml.), the bulk of the alcohol removed under reduced pressure, and the concentrated solution poured into water. The oil was extracted with ether, and the ethereal solution washed successively with 2N-sodium carbonate and water and then dried over sodium sulphate. After recovery of the solvent, the oil obtained (6 g.) solidified, on prolonged standing, to a waxy, crystalline mass which was soluble in cold methyl alcohol and light petroleum. After two fractional distillations under reduced pressure the main fraction (4 g.) had b. p. 150—152°/2 mm., m. p. 50—53°, acid value 55·4 (the alkali was gradually absorbed to give this figure), ester value 196·7 (Found: C, 68·8; H, 8·4; OMe, 15·7. A monomethyl lactonic ester, $C_{15}H_{22}O_4$, requires C, 67·5; H, 8·3; OMe, 11·7%. A dimethyl ester, $C_{16}H_{24}O_4$, requires C, 68·6; H, 8·6; OMe, 22·1%).

Action of Hydrogen Bromide on the Methyl Ester from the α-Phellendrene–Maleic Anhydride Adduct.—The methyl ester (Goodway and West, J., 1938, 2031) (4 g.), m. p. 103—104°, dissolved in a 15% solution of hydrogen bromide in glacial acetic acid (40 ml.), was heated in a sealed tube at 110—120° for 6½ hours. The acetic acid and hydrogen bromide were removed by distillation under reduced pressure and the red oily residue, which showed no tendency to crystallise, was boiled with acetyl chloride (5 ml.) for 2 hours. After standing for some weeks over solid caustic potash in a vacuum desiccator, the viscous product was triturated with a mixture of light petroleum (5 vols.) and benzene (1 vol.); the residue then crystallised. After repeated crystallisation from light petroleum–benzene (1 : 1), the white crystalline *acid* (0·3 g.) had m. p. 168—169° (Found: C, 66·5; H, 7·7; equiv., 266. A monobasic lactonic acid, $C_{14}H_{20}O_4$, requires C, 66·7; H, 7·9%; equiv., 252).

After the methyl ester had been saponified with methyl-alcoholic caustic potash, the *acid*, isolated in the usual manner and crystallised from light petroleum–benzene, had m. p. 167—169°, equiv. 273, and mixed m. p. with the above acid 168—169°.

Reaction with Tetranitromethane.—A solution of tetranitromethane (1 vol.) in AnalaR acetone (2 vols.) was added (0·2 ml.) to the compound (0·02 g.) dissolved in acetone (0·2 ml.); the colour of the solution recorded immediately remained unchanged after 30 minutes. All the observations were made on the same day with the same reagents.

Compound.	Colour with solution of tetranitromethane.
Monomethyl lactonic ester from α-phellandrene adduct	No change
Monomethyl lactonic ester from *cyclo*pentadiene adduct	,,
Lactonic acid from *cyclo*pentadiene adduct	,,
Dimethyl ester from anthracene adduct	Yellow
Dimethyl ester from myrcene adduct	Deep yellow
Dimethyl ester from isoprene adduct	,,
Dimethyl ester from $\Delta^{1:3}$-*cyclo*hexadiene adduct	Pale yellow
Mixed product from α-terpinene adduct	Yellow
Eucarvone adduct	No change
Dimethyl ester from eucarvone adduct	Pale yellow
Diethyl ester from eucarvone adduct	,,
Dimethyl ester from caryophyllene adduct	,,
Control	No change

The author thanks Dr. N. F. Goodway for his interest in this work and for kindly providing a sample of the product from the α-terpinene adduct, and is indebted to the Directors of Messrs. Stafford Allen and Sons, Ltd., for the gift of the terpenes.

THE SIR JOHN CASS INSTITUTE, LONDON, E.C. 3. [*Received, February 11th*, 1941.]

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33. *The Preparation of Some Condensation Products of* m-*Dialkylaminobenzaldehydes with Compounds containing Reactive Methylene Groups, and an Investigation of their Suitability as Photographic Sensitisers.*

By WESLEY COCKER and DENYS G. TURNER.

A number of condensation products of 6-substituted quinaldine methiodides with *m*-dimethyl- and *m*-diethyl-aminobenzaldehydes have been prepared. The compounds and also those previously described (J., 1940, 57) are of little value as photographic sensitisers.

THE value as photographic sensitisers of the condensation products of *p*-dimethylaminobenzaldehyde and the methiodides of heterocyclic bases possessing a 2-methyl group is well known (Mills and Smith, J., 1922, **121**, 2724; Smith, J., 1923, **123**, 2288). Some of the corresponding *m*-dialkylamino-compounds have been described by the present authors (*loc. cit.*) and the preparation of 6-*methyl*-, 6-*bromo*-, and 6-*methoxy*-2-m-*dimethylaminostyrylquinoline methiodides* and also 6-*methoxy*- and 6-*dimethylamino*-2-m-*diethylaminostyrylquinoline methiodides* is now recorded. These compounds and the condensation products of *m*-dimethylaminobenzaldehyde with the methiodides of α-picoline, quinaldine, 2-methylthiazole and 2-methylbenzthiazole previously described (*loc. cit.*) have been investigated spectrographically.

Spectrographic investigation was performed with a wedge spectrograph. "Ilford Ordinary" (unsensitised) plates were bathed for 5 minutes in a solution of each dye (1 part of dye in 30,000 parts of 33% alcohol). The dried plates were then exposed for various times in the spectrograph.

Only 6-methyl-2-*m*-dimethylamino- and 6-dimethylamino-2-*m*-diethylamino-styrylquinoline methiodides showed any characteristics other than those of the control plates, and these compounds only showed the slightest increase of sensitivity in the direction of the red end of the spectrum.

This absence of photosensitising action is interesting and demonstrates the necessity for a fully conjugated system between the anionoid (-$NAlk_2$) and cationoid (-$\overset{+}{N}$) centres of the molecule such as exists in the *p*-dialkylamino-substituted compounds. Consequently electromeric shifts of the type $Me_2N\overset{\curvearrowright}{-}C\overset{\curvearrowleft}{=}C\overset{\curvearrowright}{-}C\overset{\curvearrowleft}{=}\overset{+}{N}$ cannot take place. Thus, even though there are two powerful anionoid centres in 6-bromo- and 6-methoxy-2-*m*-dimethylamino- and 6-methoxy- and 6-dimethylamino-2-*m*-diethylamino-styrylquinoline methiodides with the consequent electropolar effects, the existence alone of such strong electropolar effects is insufficient to produce sensitising action, and an electron transfer system is necessary.

All attempts to prepare 6-dimethylamino-2-*m*-dimethylaminostyrylquinoline methiodide were unsuccessful and some difficulty was experienced in the preparation of the corresponding 6-methoxy-compound until the *m*-dimethylaminobenzaldehyde was twice steam-distilled in strongly alkaline conditions, followed by careful distillation in a vacuum. On the other hand, *m*-diethylaminobenzaldehyde condensed readily with 6-methoxy- and 6-dimethylamino-quinaldine methiodides, and this appears contrary to the usually accepted views on the Knoevenagel reaction. It can only be assumed that the aldehyde had developed some anti-catalyst on keeping.

Experimental.

2-m-*Dimethylaminostyryl-6-methylquinoline Methiodide.*—A mixture of 6-methylquinaldine methiodide (2 g.), *m*-dimethylaminobenzaldehyde (1 g.), alcohol (40 c.c.), and piperidine (1 c.c.) was refluxed for 6 hours and cooled. The crystalline deposit, after being washed with a little alcohol and with ether, crystallised from alcohol in small blue-black prisms (0·5 g.), m. p. 253° (Found: C, 58·5; H, 5·3. $C_{21}H_{23}N_2I$ requires C, 58·5; H, 5·3%). It gave an intense purple solution in alcohol and its absorption spectrum displayed a strong band with a maximum at 5670 A. and a smaller one at 2980 A.

6-*Bromo*-2-m-*dimethylaminostyrylquinoline methiodide*, similarly prepared from 6-bromoquinaldine methiodide (1·79 g.) (Bartow and McCollum, *J. Amer. Chem. Soc.*, 1904, **26**, 704), *m*-dimethylaminobenzaldehyde (0·7 g.), alcohol (30 c.c.), and piperidine (0·5 c.c.), crystallised from a large volume of methyl alcohol in long purple prisms (1·3 g.), m. p. 244·5° (Found: C, 48·7; H, 3·9. $C_{20}H_{20}N_2BrI$ requires C, 48·5; H, 4·0%). The dye gave a red solution in alcohol and its absorption curve showed two maxima at 2550 A. and 3910 A.

6-*Methoxy*-2-m-*dimethylaminostyrylquinoline Methiodide.*—6-*Methoxyquinaldine methiodide.* References to this compound have not been found and those to the free base are scanty. Kozlov and Gimpelvich (*J. Gen. Chem. U.S.S.R.*, 1936, **6**, 1341) prepared an oil, apparently 6-methoxyquinaldine, b. p. 176—179°/33 mm., from *p*-anisidine and acetylene in presence of cuprous and mercuric chlorides, using toluene as solvent. The following method gives the quinaldine as a white crystalline solid. *p*-Anisidine (19 g.), dissolved in concentrated hydrochloric acid, was heated for 4 hours on the water-bath with paraldehyde (25 g.). The product was cooled and poured into a large excess of dilute alkali solution, the tarry deposit extracted with ether, and the extract dried over sodium sulphate and fractionated. The fraction, b. p. 240—280°, was dissolved in hydrochloric acid and treated at 0° with an excess of sodium nitrite. After extraction with ether, the aqueous layer was basified, heated for 2 hours on the water-bath, cooled, and again extracted with ether. This extract was dried, the solvent removed, and the dark residue fractionated in a vacuum. The required 6-*methoxyquinaldine* (10 g.) was a light yellow oil, b. p. 138—139°/5 mm., which rapidly solidified on cooling in ice; it then readily crystallised with little loss from light petroleum (b. p. 40—60°) in colourless, transparent tablets, m. p. 64—65° (Found: C, 76·2; H, 6·3. $C_{11}H_{11}ON$ requires C, 76·3; H, 6·3%). The

methiodide crystallised from alcohol, in which it was sparingly soluble, in pale yellow needles, m. p. 238° (decomp.) (Found: C, 45·7; H, 4·6. $C_{13}H_{14}ONI$ requires C, 45·7; H, 4·4%).

The methiodide (2·1 g.), suspended in alcohol (30 c.c.), was refluxed for 1 hour with *m*-dimethylaminobenzaldehyde (1 g.), piperidine being used as catalyst. After a few minutes red crystals of 6-*methoxy*-2-m-*dimethylaminostyrylquinoline methiodide* were obtained. After cooling, these were collected, washed with alcohol and ether, and recrystallised from a large bulk of methyl alcohol, forming long, red, felted prisms, m. p. 235° (decomp.) (Found: C, 56·8; H, 4·9. $C_{21}H_{23}ON_2I$ requires C, 56·5; H, 5·2%). The dye gave an orange solution in alcohol, and an absorption curve with a maximum at 3925 A. and lower maxima at 3150 A. and 2825 A.

6-*Methoxy*-2-m-*diethylaminostyrylquinoline methiodide* crystallised from a large volume of methyl alcohol in dark red needles or long prisms with a violet reflex, m. p. 240° (decomp.) (Found: C, 58·3; H, 6·0. $C_{23}H_{27}ON_2I$ requires C, 58·2; H, 5·7%).

6-*Dimethylamino*-2-m-*diethylaminostyrylquinoline Methiodide*.—6-Dimethylaminoquinaldine methiodide (A) was prepared by Barbier's method (*Bull. Soc. chim.*, 1920, **27**, 427), who separated it from its isomer, quinaldinetetramethylammonium iodide (B), by fractional crystallisation from alcohol. He described (A) as red-orange crystals, m. p. 230°, and (B) as pale orange leaflets, m. p. 190°. We found that (A) crystallised from alcohol in deep orange needles, m. p. 268—269°, and (B) from the same solvent in colourless plates, m. p. 199—200°. However, when the latter compound was heated at 200—205° for 10 minutes, it isomerised to compound (A) and then gave m. p. and mixed m. p. 268—269°. The best method of separation was by crystallisation from hot water, in which (B) was readily soluble and (A) only sparingly soluble [Found: (A) C, 47·6; H, 5·2; I, 38·1; (B) C, 47·7; H, 5·1. Calc. for $C_{13}H_{17}N_2I$: C, 47·6; H, 5·2; I, 38·6%].

All attempts to condense (A) or (B) with *m*-dimethylaminobenzaldehyde were unsuccessful. (B) was recovered quantitatively unchanged as expected, and (A) gave a deep green solution from which a dark micro-crystalline powder was obtained. Recrystallisation from alcohol effected no apparent purification and analysis indicated the substance to be largely (A). By treatment with charcoal in hot alcohol (A) was recovered in almost pure condition.

6-*Dimethylamino*-2-m-*diethylaminostyrylquinoline methiodide* crystallised from dilute alcohol in long, deep red prisms or needles with a bronze lustre, m. p. 220—221° (Found: C, 59·3; H, 6·5. $C_{24}H_{30}N_2I$ requires C, 59·1; H, 6·2%).

The authors thank the Chemical Society for a grant to one of them (D. G. T.) and Dr. R. Raper for assistance with the spectrograph.

KING'S COLLEGE, UNIVERSITY OF DURHAM. [*Received, January 7th*, 1941.]

NOTE.

The Formation of Trichloroacetic Acid from Perchloroethylene by Atmospheric Oxidation. By KENNETH C. BAILEY and W. S. E. HICKSON.

WHILE seeking means of stabilising perchloroethylene against atmospheric oxidation (J., 1939, 767), one of us observed that carbonyl chloride was not the sole primary oxidation product, since the hydrochloric acid and carbonic acid formed on hydrolysis of the carbonyl chloride were always accompanied by an acid whose titration value was about half that of the hydrochloric acid. Glass bottles (250 c.c.), each containing 10 c.c. of perchloroethylene and 0·2 c.c. of water, were exposed to sunlight for about 4 months. The contents were then shaken with water for about ½ hour to complete hydrolysis, and the aqueous extract was evaporated in an exhausted desiccator. The solution deposited crystals (about 2 g.), the properties and colour reactions of which agreed exactly with those of trichloroacetic acid as described by Ware (*Chemist and Druggist*, 1935, **123**, 282). This was confirmed by titration (Found: *M*, 164·6. Calc. for $CCl_3{\cdot}CO_2H$; *M*, 163·4), and by esterification with ethyl alcohol. The ester, which had the characteristics of ethyl trichloroacetate, on treatment with aqueous ammonia deposited a sparingly soluble amide [m. p. 140·8°; mixed m. p. with authentic trichloroacetamide (m. p. 141°) 141·0°].

Trichloroacetic acid has been observed when perchloroethylene is oxidised by peracetic acid (Prileshaeva and Prileshaev, *J. Gen. Chem. Russia*, 1939, **9**, 1766), and it is possible that in our experiments the real oxidising agent may be ozone or hydrogen peroxide, formed under the action of sunlight.—TRINITY COLLEGE, DUBLIN. [*Received, December 2nd*, 1940.]

Eleventh Report of the Committee on Atomic Weights of the International Union of Chemistry.

By G. P. BAXTER (Chairman), M. GUICHARD, O. HÖNIGSCHMID, and R. WHYTLAW-GRAY.

The following report of the Committee covers the twelve-month period, September 30th, 1939, to September 30th, 1940.* Only one change in the table of atomic weights has been adopted, in the case of holmium from 163·5 to 164·94.

Carbon and Sulphur.—Moles, Toral, and Escribano (*Trans. Faraday Soc.*, 1939, **35**, 1439) have redetermined the limiting densities of oxygen, ethylene, carbon dioxide, sulphur dioxide, and hydrogen sulphide, using an improved volumeter, in which the globes held more than 2 l. each. The gases were chemically purified and dried, and finally fractionally distilled or sublimed (carbon dioxide). In the following tables the corrected values of Density/Pressure are given. Adsorption corrections, as determined by Crespi, have been applied.

THURINGIAN GLASS GLOBES.

P = 1 atm.	0·75 atm.	0·67 atm.	0·50 atm.	0·33 atm.	0·25 atm.
		Oxygen.			
1·42895	1·42856	1·42856	1·42829	1·42810	1·42802
1·42898	1·42860	1·42855	1·42829	1·42802	1·42789
1·42895	1·42864	1·42840	1·42828	1·42800	1·42802
1·42894	1·42859	1·42854	1·42830	1·42806	1·42792
1·42892			1·42826		1·42801
					1·42792
Average 1·42895	1·42860	1·42851	1·42828	1·42805	1·42796
		Ethylene.			
1·26037	1·25807	1·25732	1·25582	1·25431	1·25341
1·26035	1·25809	1·25730	1·25572	1·25420	1·25350
1·26041	1·25810	1·25730	1·25577	1·25425	1·25358
1·26033	1·25809	1·25732	1·25579	1·25433	1·25346
1·26033	1·25805	1·25730	1·25571	1·25429	1·25351
1·26036	1·25804	1·25733	1·25583	1·25430	1·25349
			1·25578		1·25344
			1·25586		1·25363
			1·25574		
Average 1·26036	1·25807	1·25731	1·25578	1·25428	1·25350
		Sulphur dioxide.			
2·92658		2·90377	2·89233	2·88090	2·87515
2·92654		2·90362	2·89226	2·88085	2·87518
2·92652		2·90357	2·89230	2·88069	2·87513
2·92654		2·90379	2·89220	2·88070	2·87497
2·92653		2·90367	2·89223	2·88085	2·87498
2·92659		2·90374	2·89231	2·88083	2·87522
2·92653		2·90367	2·89227	2·88084	
				2·88080	
Average 2·92655		2·90369	2·89227	2·88081	2·87511

JENA GLASS GLOBES.

Oxygen.		*Carbon dioxide.*		*Sulphur dioxide.*	
P = 1 atm.	P = 0·5 atm.	P = 1 atm.	P = 0·5 atm.	P = 1 atm.	P = 0·5 atm.
1·429000	1·42832	1·976896	1·97016	2·92658	2·89229
1·428937	1·42829	1·97695	1·97011	2·92657	2·89233
1·428963	1·42828	1·976935	1·97015	2·92654	2·89227
1·428921	1·42830	1·97694	1·97013	2·92652	2·89234
1·428952	1·42828	1·97695	1·97011	2·92656	2·89237
1·428910	1·42828	1·97693	1·97016	2·92654	2·89226
1·428916	1·42831	1·97694	1·97014	2·92654	2·89230
1·428943					
1·428954					
Av. 1·428944	1·42829	1·97693	1·97017	2·92655	2·89231

* Authors of papers bearing on the subject are requested to send copies to each of the four members of the Committee at the earliest possible moment: Prof. G. P. Baxter, Coolidge Laboratory, Harvard University, Cambridge, Mass., U.S.A.; Prof. M. Guichard, Faculté des Sciences, Sorbonne, Paris, France; Prof. O. Hönigschmid, Sofienstrasse 9/2, Munich, Germany; Prof. R. Whytlaw-Gray, University of Leeds, Leeds, England.

Hydrogen sulphide was investigated by Regnault's globe method.

Hydrogen sulphide.

$P = 1$ atm.			$P = 0{\cdot}5$ atm.		
Globe I.	Globe II.		Globe I.	Globe II.	
1·53854		1·53846	1·53834		1·52948
1·53836	1·53843	1·53843	1·53840	1·52935	1·52941
1·53833	1·53832		1·53848	1·52949	1·52936
1·53834	1·53851	1·53843	1·53850	1·52942	1·52934
1·53837	1·53849	1·53849	1·53848	1·52942	1·52944
1·53843	1·53841	Av. 1·53842	1·53844	Av. 1·52942	1·52941
		1·53843		1·52941	

The following equations have been derived for Density/Pressure values.

Oxygen	D/P	$1{\cdot}427619 + 0{\cdot}0001326\,P$
Ethylene	D/P	$1{\cdot}251223 + 0{\cdot}009134\,P$
Sulphur dioxide	D/P	$2{\cdot}857957 + 0{\cdot}068593\,P$

These and the data for carbon dioxide and hydrogen sulphide give the following molecular and atomic weights.

	Mol. wt.	At. wt., C.	At. wt., S.
Ethylene	28·046	12·007	
Sulphur dioxide	64·061		32·061
Carbon dioxide	44·008	12·008	
Hydrogen sulphide	34·079		32·063

Phosphorus.—Hönigschmid and Hirschbold-Wittner (*Z. anorg. Chem.*, 1940, **243**, 355) have compared phosphorus oxybromide with silver. The oxybromide was prepared by refluxing the pentabromide with phosphorus pentoxide. After distillation, in order to remove tribromide, the material was again refluxed with bromine and pentoxide. It was then fractionally distilled many times in an exhausted all-glass system and fractions for analysis were collected in sealed glass bulbs. After six distillations with rejection of substantial light fractions the main portion was divided into light (H), middle (M and M_1), and heavy (E) fractions. The light fractions rejected earlier were combined and fractionated and the heavy fraction (V) was analysed.

The bulbs were weighed in air and under water, broken under aqueous ammonia, and the glass was collected for weighing. After acidification of the solution it was compared with weighed quantities of pure silver by the usual nephelometric process. Finally the silver bromide was collected and weighed. Weights are corrected to vacuum.

The Atomic Weight of Phosphorus.

Fraction.	$POBr_3$, g.	Ag, g.	$POBr_3 : 3Ag$.	At. wt., P.	AgBr, g.	$POBr_3 : 3AgBr$.	At. wt., P.
V	5·54550	6·25967	0·885909	30·968	10·89645	0·508927	30·975
	5·16219	5·82671	0·885928	30·974			
	5·30583	5·98897	0·885934	30·976			
		Average	0·885924	30·973		0·508927	30·975
H	4·70003	5·30521	0·885927	30·974	9·23529	0·508921	30·972
H	4·46732	5·04259	0·885918	30·971	8·77784	0·508932	30·978
H	4·58384	5·17404	0·885931	30·975	9·00649	0·508949	30·988
		Average	0·885925	30·973		0·508934	30·979
M	4·64994	5·24880	0·885905	30·967	9·13691	0·508918	30·970
M	5·20581				10·22916	0·508919	30·971
M	5·45761	6·16028	0·885935	30·976	10·72369	0·508930	30·977
M	5·07426	5·72777	0·885905	30·966	9·97123	0·508890	30·955
M	6·31287	7·12578	0·885920	30·971	12·40460	0·508914	30·968
		Average	0·885916	30·970		0·508914	30·968
M	5·83139	6·58233	0·885916	30·970	11·45824	0·508925	30·974
M	6·43986	7·26901	0·885934	30·976	12·65365	0·508933	30·979
M	5·70576	6·44029	0·885948	30·980	11·21107	0·508940	30·983
M	5·70714	6·44202	0·885924	30·972	11·21406	0·508927	30·975
M	5·31468	5·99898	0·885931	30·975	10·44279	0·508933	30·979
		Average	0·885931	30·975		0·508932	30·978
E	5·07335	5·72633	0·885969	30·987	9·96817	0·508955	30·991
E	5·05071	5·70099	0·885936	30·976	9·92415	0·508931	30·978
E	5·95421	6·72069	0·885952	30·982	11·69909	0·508946	30·986
		Average	0·885952	30·982		0·508944	30·985
		Average of all	0·885929	30·974		0·508930	30·976
		Average, omitting Fraction E,	0·885924	30·973		0·508925	30·975

Since sample E appears to be slightly different in composition from the others, the authors prefer the average obtained with the other four samples, 30·974. This value is slightly lower than that found recently by Hönigschmid and Menn (30·978) by analysis of the oxychloride, but the authors feel that the latter value is more reliable.

Potassium.—Baxter and Harrington (*J. Amer. Chem. Soc.*, 1940, **62**, 1836) have compared potassium chloride with silver. Purification of the potassium salt consisted in crystallisation of the chlorate, perchlorate, and chloride. Fusion in an atmosphere of hydrogen containing hydrogen chloride preceded the weighing of the salt. The comparison with silver followed conventional nephelometric technique. Vacuum weights are given.

THE ATOMIC WEIGHT OF POTASSIUM.

KCl, g.	Ag, g.	KCl : Ag.	Atomic weight of K.
4·88482	7·06819	0·691099	39·099
4·08265	5·90751	0·691094	39·098
8·52040	12·32907	0·691082	39·097
8·62997	12·48749	0·691089	39·098
8·77749	12·70096	0·691089	39·098
	Average	0·691085	39·098

Iodine.—Baxter and Kelley (*J. Amer. Chem. Soc.*, 1940, **62**, 1824) by displacement of liquids have found the following values for the specific gravity ($d_4^{25°}$) of iodine pentoxide: (xylene) 4·907, (mesitylene) 4·905, (kerosene) 4·952, (chlorobenzene) 4·980.

All these values are lower than that recently found by Moles and Villan but higher than the older value found by Baxter and Tilley. Of the above values, that found with chlorobenzene is preferred. By displacement of air the value 4·98 was found.

Since with the use of this value no correction for air adsorption (0·001%) is necessary but the vacuum correction is 0·001 smaller, the weights of iodine pentoxide given by Baxter and others in various recent investigations need no correction, in contradiction to the claim of Moles (see Report of this Committee for 1938).

Baxter and Titus (*J. Amer. Chem. Soc.*, 1940, **62**, 1826) have redetermined the ratio of silver iodide to silver chloride by heating the former substance in chlorine in a special quartz weighing tube. Silver was purified by (A) crystallisation of silver nitrate, reduction, and fusion on lime, and (B) precipitation as chloride and as metal, electrolytic transport, and fusion. Iodine was purified (I and II) by distillation from potassium iodide and sublimation in air over hot platinum, (III) by crystallisation as iodic acid, decomposition and sublimation. To prepare silver iodide, a solution of the silver in nitric acid was added to a solution of hydriodic acid made by dissolving iodine in distilled hydrazine. The silver iodide was prepared for weighing by heating to fusion in the quartz reaction tube in a stream of air laden with iodine and then in pure air. After being weighed, the salt was heated, at first gently, later more strongly until fused, in a current of chlorine, and then in air to displace the chlorine. Prolonged heating of silver iodide in air was found to induce slight decomposition. In two experiments the silver iodide was converted into silver bromide and weighed before conversion into chloride.

Vacuum weights are given in the following table.

THE ATOMIC WEIGHT OF IODINE.

Sample of Ag.	Sample of I_2.	AgI, g.	AgCl, g.	AgI : AgCl.	At. wt. of iodine.	AgBr, g.	AgI : AgBr.	At. wt. of iodine
B	I	19·29812	11·78127	1·638033	126·911			
B	I	18·56636	11·33416	1·638089	126·919			
B	I	17·61333	10·75259	1·638055	126·914			
B	I	17·28888	10·55452	1·638055	126·914			
A	II	24·77025	15·12167	1·638063	126·915	19·81186	1·250274	126·916
A	II	26·53177	16·19680	1·638087	126·918	21·22030	1·250301	126·922
A	III	27·13226	16·56361	1·638064	126·915			
A	III	26·72367	16·31365	1·638117	126·923			
A	III	23·26211	14·20115	1·638044	126·912			
A	III	24·35477	14·86829	1·638034	126·911			
A	III	23·82804	14·54653	1·638057	126·914			
A	III	23·54677	14·37480	1·638059	126·914			
			Average	1·638062	126·915		1·250288	126·919

THE ATOMIC WEIGHT OF BROMINE.

AgBr, g.	AgCl, g.	AgBr : AgCl.	At. wt. of bromine.
19·81186	15·12167	1·310163	79·915
21·22030	16·19680	1·310154	79·914

Baxter and Lundstedt (*J. Amer. Chem. Soc.*, 1940, **62**, 1829) have determined the ratio of silver to silver iodide and of silver iodide to silver chloride. Silver was purified by (A) three electrolyses with a dissolving anode, (B) an additional electrolysis of (A), and (C) an additional electrolysis of (B). Spectroscopically these three specimens appeared identical, although the residual electrolytes proved to contain small but diminishing proportions of impurities. Sample (D) was purified by crystallisation of silver nitrate, reduction with formate, and one electrolytic transport; sample (E) by precipitation as chloride, reduction with formate, and one electrolytic transport. All five samples were finally fused in hydrogen on a pure lime support. Quantitative synthesis of silver chloride much as with the iodide gave the following results (vacuum weights):

THE ATOMIC WEIGHT OF CHLORINE.

Sample of Ag.	Ag, g.	AgCl, g.	Ag : AgCl.	Atomic wt. of Cl.
A	9·00350	11·96264	0·752635	35·457
B	10·40823	13·82954	0·752609	35·461
D	8·99809	11·95549	0·752632	35·457

Iodine was purified as follows: Sample I, three distillations from aqueous potassium iodide, made from a portion of the partially purified material in each case, and distillation in a current of oxygen over red hot platinum; sample II, decomposition of sodium iodate, made from recrystallised iodic acid, and distillation with steam.

Weighed quantities of silver were dissolved in nitric acid and precipitated with an excess of iodide made by reduction of iodine with hydrazine. The precipitate was washed with dilute nitric acid and collected on a weighed platinum sponge crucible. After being weighed, it was transferred to a special quartz weighing vessel and the change in weight on fusion in iodine was found. The filtrate and washings were evaporated, and the dissolved silver iodide recovered. Weights are corrected to the vacuum standard.

THE ATOMIC WEIGHT OF IODINE.

Sample of Ag.	Sample of I.	Ag, g.	AgI, g.	I : Ag.	Atomic wt. of I.
A	I	9·11927	19·84738	1·176422	126·9124
A	I	10·48742	22·82508	1·176425	126·9127
A	II	10·14331	22·07589	1·176399	126·9099
A	II	9·00775	19·60483	1·176440	126·9143
D	II	9·53995	20·76333	1·176461	126·9166
D	I	9·78621	21·29919	1·176449	126·9153
B	II	9·04011	19·67510	1·176423	126·9125
B	I	9·99801	21·76008	1·176441	126·9144
A	II	9·14163	19·89601	1·176418	126·9120
B	II	10·00740	21·78024	1·176413	126·9114
D	I	10·47710	22·80288	1·176450	126·9154
B	I	9·52800	20·73713	1·176441	126·9144
C	I	9·89577	21·53744	1·176429	126·9132
C	I	10·47841	22·80542	1·176420	126·9122
C	I	10·44012	22·72226	1·176437	126·9140
E	I	8·47813	18·45227	1·176455	126·9160
			Average	1·176433	126·9135

The weighed silver iodide obtained in many of the experiments was converted into silver chloride as in the foregoing experiments of Baxter and Titus.

THE ATOMIC WEIGHT OF IODINE.

AgI, g.	AgCl, g.	AgI : AgCl.	Atomic wt. of I.	AgI, g.	AgCl, g.	AgI : AgCl.	Atomic wt. of I.
21·24430	12·96904	1·638078	126·917	21·28690	12·99508	1·638073	126·916
21·70430	13·24993	1·638069	126·916	22·65326	13·82927	1·638066	126·915
19·80231	12·08877	1·638075	126·917	22·47202	13·71853	1·638078	126·917
21·61515	13·19557	1·638061	126·915	18·19991	11·11055	1·638075	126·917
22·69504	13·85480	1·638063	126·915		Average	1·638071	126·916
20·61686	12·58599	1·638080	126·917				

If the mean of all the silver iodide syntheses, 126·913(5), is combined with the mean of all the above silver iodide–silver chloride conversions, 126·915(6), the average value 126·914 is obtained. With the conversion factor 1·000275 this atomic weight yields the packing fraction $-3{\cdot}0 \times 10^{-4}$, while mass spectrograph data seem to indicate a value slightly larger than -4×10^{-4}.

Combination of recent experimental ratios involving iodine pentoxide yields values tending to support the above average:

Assumed.		At. wt. I.
O = 16·0000	$2Ag/I_2O_5 = 0{\cdot}646236$ and $Ag/I = 0{\cdot}849904$	126·920
O = 16·0000	$6AsCl_3/I_2O_5 = 3{\cdot}25818$ and $AsCl_3/I_2 = 0{\cdot}714191$	126·905
Ag = 107·880	$6AsCl_3/I_2O_5 = 3{\cdot}25818$ and $AsCl_3/3Ag = 0{\cdot}6560128$	126·915
Ag = 107·880	$AsCl_3/I_2 = 0{\cdot}714191$ and $AsCl_3/3Ag = 0{\cdot}560128$	126·913
Ag = 107·880	$I_2O_5/Na_2CO_3 = 3{\cdot}14950$ and $2Ag/Na_2CO_3 = 2{\cdot}03556$	126·916
	Average	126·914

Cæsium.—Baxter and Harrington (*J. Amer. Chem. Soc.*, 1940, **62**, 1834) have compared cæsium chloride with silver. Nearly pure cæsium nitrate remaining from an earlier investigation (Baxter and Thomas) was fractionally crystallised through twenty series with occasional rejection of the most soluble fraction until rubidium and potassium could not be detected spectroscopically in the most soluble fraction. The three least soluble fractions of the twentieth series were combined and precipitated as perchlorate, and this salt was crystallised three times in platinum vessels. Conversion into chloride by thermal decomposition in platinum followed, and the chloride was crystallised four times in platinum in the presence of a small quantity of hydrazine to prevent attack of the platinum. The purified salt was prepared for weighing by drying and fusion in a platinum boat in an atmosphere of dry hydrogen and hydrogen chloride. After being weighed, the salt was dissolved and compared with weighed quantities of silver in the usual way, with the aid of a nephelometer. Tests showed the fused salt to be neutral and free from hydrazine and ammonia.

Weights are corrected to vacuum.

The Atomic Weight of Cæsium.

CsCl, g.	Ag, g.	CsCl : Ag.	Atomic wt. of cæsium.	CsCl, g.	Ag, g.	CsCl : Ag.	Atomic wt. of cæsium.
15·73190	10·08001	1·560703	132·912	15·19052	9·73300	1·560723	132·914
17·98374	11·52285	1·560702	132·912	17·58470	11·26723	1·560694	132·911
11·82978	7·45177	1·560674	132·909	18·32957	11·74473	1·560663	132·907
18·23097	11·68119	1·560712	132·913	16·59433	10·63256	1·560709	132·912
16·45522	10·54340	1·560713	132·913	17·53781	11·23671	1·560760	132·918
14·74725	9·44889	1·560739	132·916		Average	1·560709	132·912(5)
17·06711	10·93545	1·560714	132·913				

With the conversion factor 1·000275, the packing fraction of cæsium is calculated to be $-3{\cdot}79 \times 10^{-4}$, which compares favourably with the physical values $-3{\cdot}8 \times 10^{-4}$ (Dempster), $-4{\cdot}0 \times 10^{-4}$ (Hahn, Flügge, and Mattauch), and $-3{\cdot}8 \times 10^{-4}$ (Aston).

Holmium.—Hönigschmid and Hirschbold-Wittner (*Z. anorg. Chem.*, 1940, **244**, 63) have analysed holmium chloride by comparison with silver. The holmium material had been purified by Feit (*ibid.*, 1940, **243**, 276) by fractionation as bromate and as basic nitrate. *X*-Ray analysis by Noddack showed the following atom per cent. of rare-earth impurity: yttrium, 0·013; erbium, 0·04; dysprosium, 0·03; other rare earths, 0·02. After repeated precipitation of the hydroxide and oxalate, the chloride was prepared by solution of the oxide in hydrochloric acid and the chloride was twice precipitated by saturating the aqueous solution with hydrogen chloride. Drying was effected by gradually heating the chloride, ultimately to fusion in a current of hydrogen chloride. Comparison with silver in the usual way with a nephelometer followed and the silver chloride was collected. Weights are corrected to vacuum.

THE ATOMIC WEIGHT OF HOLMIUM.

Ho, g.	Ag, g.	$HoCl_3$: 3Ag.	At. wt., Ho.	AgCl, g.	$HoCl_3$: 3AgCl.	At. wt., Ho.
2·20620				3·49683	0·63092	164·929
2·16354	2·58091	0·83829	164·932	3·42918	0·63092	164·932
2·22679	2·65622	0·83833	164·946	3·52933	0·63094	164·940
1·44966	1·72930	0·83829	164·934	2·29770	0·63092	164·931
3·18194	3·79581	0·83828	164·929	5·04342	0·63091	164·927
4·74923	5·66553	0·83827	164·926	7·52767	0·63090	164·924
	Average	0·83829	164·933		0·63092	164·930

Correction for the yttrium content raises the experimental average to 164·94. Since holmium appears to be a simple element, the atomic weight may be computed from the mass number with the use of the conversion factor and the packing fraction $-0{\cdot}8 \times 10^{-4}$. The physical value 164·94 thus agrees exactly with the above value, and is adopted for the table.

Hartley, Henry, and Whytlaw-Gray (*Trans. Faraday Soc.*, 1939, **35**, 1452) have measured experimentally the adsorption of certain gases on fused silica surfaces, and find this to be only a small fraction of that on glass surfaces. In the following table are given the values in ml. $\times 10^{-6}$ per cm.^{2} at 760 mm. and 21° :

Gas	SO_2	N_2O	C_2H_4	CO_2	N_2	CO	A	O_2
Ml. $\times 10^{-6}$/cm.^{2}	11·0	1·61	1·51	1·44	0·74	0·44	0·42	0·20
Unimolecular layer, %	50			6				0·7

Even with sulphur dioxide the effect upon the measurements with a micro-displacement balance with uncompensated bulb of 1·7 ml. is only 1×10^{-5}, and of course disappears if the two arms of the balance expose equal surfaces.

Bloom due to condensed silica vapour during the construction of the silica apparatus was found to increase the quantity of adsorbed gas to many times its value on clean surfaces.

Attention is called to the marked discrepancies between several chemical values in the atomic weight table and the corresponding values based on mass-spectrographic evidence. In most of these cases the element is simple so far as is known, so that the atomic weight cannot be far from the mass number. Although it seems unlikely that new physical evidence will alter the mass spectrographic values materially, the Committee hesitates to change the values in the table at the present time. The packing fractions used below are taken from the table of Hahn, Flügge, and Mattauch (*Ber.*, 1940, **73**, *A*, 1), and the value 1·000275 is used for the conversion factor.

Scandium. Simple element, packing fraction $-8{\cdot}9 \times 10^{-4}$, physical atomic weight 44·96.

Terbium. Simple element, packing fraction $-1{\cdot}4 \times 10^{-4}$, physical atomic weight 158·93.

Thulium. Simple element, packing fraction $-0{\cdot}4 \times 10^{-4}$, physical atomic weight 168·95.

Iridium. Abundance ratio $^{191}Ir/^{193}Ir = 38{\cdot}5/61{\cdot}5$, packing fraction $+2{\cdot}1 \times 10^{-4}$, physical atomic weight 192·22. In this case the chemical atomic weight 193·1 appears to be impossible.

Gold. Simple element, packing fraction $+2{\cdot}0 \times 10^{-4}$, physical atomic weight 196·99.

Hönigschmid (*Angew. Chem.*, 1940, **53**, 177) reviews the determinations of atomic weights carried out during the past thirty years in his laboratory at Munich.

INTERNATIONAL ATOMIC WEIGHTS.

1941.

	Symbol.	Atomic Number.	Atomic Weight.
Aluminium	Al	13	26·97
Antimony	Sb	51	121·76
Argon	A	18	39·944
Arsenic	As	33	74·91
Barium	Ba	56	137·36
Beryllium	Be	4	9·02
Bismuth	Bi	83	209·00
Boron	B	5	10·82
Bromine	Br	35	79·916
Cadmium	Cd	48	112·41
Cæsium	Cs	55	132·91
Calcium	Ca	20	40·08
Carbon	C	6	12·010
Cerium	Ce	58	140·13
Chlorine	Cl	17	35·457
Chromium	Cr	24	52·01
Cobalt	Co	27	58·94
Copper	Cu	29	63·57
Dysprosium	Dy	66	162·46
Erbium	Er	68	167·2
Europium	Eu	63	152·0
Fluorine	F	9	19·00
Gadolinium	Gd	64	156·9
Gallium	Ga	31	69·72
Germanium	Ge	32	72·60
Gold	Au	79	197·2
Hafnium	Hf	72	178·6
Helium	He	2	4·003
Holmium	Ho	67	164·94
Hydrogen	H	1	1·0080
Indium	In	49	114·76
Iodine	I	53	126·92
Iridium	Ir	77	193·1
Iron	Fe	26	55·85
Krypton	Kr	36	83·7
Lanthanum	La	57	138·92
Lead	Pb	82	207·21
Lithium	Li	3	6·940
Lutecium	Lu	71	174·99
Magnesium	Mg	12	24·32
Manganese	Mn	25	54·93
Mercury	Hg	80	200·61
Molybdenum	Mo	42	95·95
Neodymium	Nd	60	144·27
Neon	Ne	10	20·183
Nickel	Ni	28	58·69
Niobium (Columbium)	Nb (Cb)	41	92·91
Nitrogen	N	7	14·008
Osmium	Os	76	190·2
Oxygen	O	8	16·0000
Palladium	Pd	46	106·7
Phosphorus	P	15	30·98
Platinum	Pt	78	195·23
Potassium	K	19	39·096
Praseodymium	Pr	59	140·92
Protoactinium	Pa	91	231
Radium	Ra	88	226·05
Radon	Rn	86	222
Rhenium	Re	75	186·31
Rhodium	Rh	45	102·91
Rubidium	Rb	37	85·48
Ruthenium	Ru	44	101·7
Samarium	Sm	62	150·43
Scandium	Sc	21	45·10
Selenium	Se	34	78·96
Silicon	Si	14	28·06
Silver	Ag	47	107·880
Sodium	Na	11	22·997
Strontium	Sr	38	87·63
Sulphur	S	16	32·06
Tantalum	Ta	73	180·88
Tellurium	Te	52	127·61
Terbium	Tb	65	159·2
Thallium	Tl	81	204·39
Thorium	Th	90	232·12
Thulium	Tm	69	169·4
Tin	Sn	50	118·70
Titanium	Ti	22	47·90
Tungsten	W	74	183·92
Uranium	U	92	238·07
Vanadium	V	23	50·95
Xenon	Xe	54	131·3
Ytterbium	Yb	70	173·04
Yttrium	Y	39	88·92
Zinc	Zn	30	65·38
Zirconium	Zr	40	91·22

34. *The Adamkiewicz, Hopkins and Cole, and Rosenheim Tests for Tryptophan. An Investigation of the Configuration of the Organic Molecule responsible for the Colour Formation and its Bearing on the Constitution of Yohimbine, with a Note on the Action of Formaldehyde on Tryptophan.*

By Douglas Graham Harvey, Eric John Miller, and William Robson.

If to an aqueous solution of 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid,* concentrated sulphuric acid containing a trace of an oxidising agent is added so that the two liquids do not mix, the play of colours obtained at their zone of contact is similar in all respects to that obtained when tryptophan is subjected to the Adamkiewicz procedure as modified by Hopkins and Cole (*Proc. Roy. Soc.*, 1901, **68**, 21) and by Rosenheim (*Biochem. J.*, 1906, **1**, 233).

Evidence is advanced that the reaction, as described by these authors, consists of two stages : (1) the formation of 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid or a derivative thereof, (2) the oxidation of the latter substance to the blue pigment which is characteristic of the reaction.

The colour reaction of 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid with concentrated sulphuric acid containing an oxidising agent, and its use for detecting the presence of oxidising agents in sulphuric acids of commerce, are described.

Only those compounds possessing the structure of 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid have been found to give the colour reaction mentioned when treated in the above manner.

Yohimbine behaves towards concentrated sulphuric acid containing an oxidising agent in the same way as 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid. It would thus appear that the carbomethoxy-group present in the yohimbine molecule is at C_5 † (V) and not at C_{16} as postulated by Hahn, Kappes, and Ludewig (*Ber.*, 1934, **67**, 686).

That a dilute aqueous solution of egg-white, when added drop by drop to concentrated sulphuric acid, produces a range of colours starting from green and passing through yellow, orange, red, and ending in violet, was first shown by Adamkiewicz (*Pfluger's Arch.*, 1874, **9**, 156). He found, moreover, that whilst the colour obtained depended upon the concentration of the protein in the final mixture, if the egg-white had been previously treated with glacial acetic acid, only a violet colour resulted. It was Adamkiewicz's view that the coloured products arose from the interaction of substances liberated from the protein by the sulphuric acid and that the acetic acid only modified the reaction.

Udransky's view (*Z. physiol. Chem.*, 1888, **12**, 395) that one of the substances involved in the colour formation was furfural was negatived by the work of Hopkins and Cole (*loc. cit.*), who showed that the reaction occurred only when the acetic acid was impure, the impurity concerned being glyoxylic acid.

That glyoxylic acid was responsible for the reaction was doubted by Rosenheim (*loc. cit.*), who emphasised that whilst a typical Adamkiewicz reaction could be obtained by the addition of " commercial " sulphuric acid to a protein or a tryptophan solution previously treated with a minimum amount of formaldehyde, no reaction could be obtained if the sulphuric acid employed was pure. Rosenheim then demonstrated that the presence of an oxidising agent, *e.g.*, ferric chloride, was a necessary adjunct for the test. These findings were confirmed in part by Dakin (*J. Biol. Chem.*, 1906, **2**, 289), who nevertheless supported the view that the impurity in the acetic acid in question was glyoxylic acid.

* Named and numbered in accordance with the suggestion of Gulland, Robinson, Scott, and Thornley (J., 1929, 1924), adopted by King and Stiller (J., 1937, 466) and by Henry (" Plant Alkaloids," 1939, p. 464).

† The numbering of the carbon atoms in the yohimbine skeleton is that proposed by Barger and Scholz (*Helv. Chim. Acta*, 1933, **16**, 1343). So far as the carboline fraction of this molecule is concerned, it differs from that suggested by Gulland *et al.* referred to above.

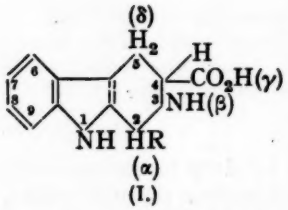
He, moreover, contended that pure glyoxylic acid reacted with tryptophan and pure sulphuric acid to give the characteristic colour.

Rosenheim's contention that the constituent of impure acetic acid which reacted with tryptophan was formaldehyde found a supporter in Voisenet (*Compt. rend.*, 1918, **166**, 789), who concluded that the pigments obtained by the Hopkins and Cole and by the Rosenheim techniques were the same substance.

In the meantime, Mottram (*Biochem. J.*, 1913, **7**, 249) had described a failure of the glyoxylic acid test as being due to the presence of an excess of oxidising agent in the sulphuric acid employed, a finding confirmed by Breidhal (*Biochem. J.*, 1915, **9**, 36), who showed that such acids could be used for the test after they had been treated with suitable amounts of reducing agents.

The realisation that the Adamkiewicz reaction might be made the basis of a method for the estimation of the tryptophan content of protein led Fearon (*Biochem. J.*, 1920, **14**, 548) to investigate the mode of formation of the blue pigment. Showing that the tests described by Hopkins and Cole and by Rosenheim depended on the use of glyoxylic acid and formaldehyde respectively, he stated that in each case two distinct coloured derivatives could be formed according to the amount of the reactant used. One product was red and the other blue, the latter arising when three molecules of formaldehyde reacted with two molecules of the amino-acid. The formula which he put forward for the latter compound was based on rather meagre evidence.

In a recent series of papers by various authors (Hahn, Barwald, Schales, and Werner, *Annalen*, 1935, **520**, 107; Hahn and Werner, *ibid.*, p. 123; Jacobs and Craig, *J. Biol. Chem.*, 1936, **113**, 759; Wadsworth and Pangborne, *ibid.*, 1936, **116**, 423; Harvey and Robson, J., 1938, 97) it has been amply demonstrated that tryptophan condenses with simple aliphatic aldehydes in aqueous solution over a wide range of p_H to yield 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acids of the general formula (I). From the extreme ease with which carboline formation proceeds—it was shown by Harvey and Robson (*loc. cit.*) that the corresponding 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid crystallises overnight from a concentrated aqueous mixture of molecular quantities of tryptophan and acetaldehyde kept at room temperature—it appears reasonable to assume that this reaction forms the first stage of the Adamkiewicz test for tryptophan. Should this hypothesis be correct, then, in the light of Rosenheim's findings, the second stage would consist in the oxidation of the carboline formed in the first stage.



(I.)

That such an interpretation of the course of the reaction is probably correct was shown as follows: When pure concentrated sulphuric acid is run into a test-tube containing a dilute acid solution of 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid in such a way that the two liquids do not mix, no colour develops at their zone of contact. Should the sulphuric acid, however, contain a trace of an oxidising agent, a play of colours is obtained at the junction of the liquids similar in every respect to that seen when tryptophan is submitted to the Hopkins and Cole and the Rosenheim reactions.

Similar findings were obtained in a slightly different way. For example, when a crystal of 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid was dropped into pure sulphuric acid, no colour development occurred. On the other hand, when the same compound was added to pure acid containing an oxidising agent, hereafter called the " reagent ", a blue colour commenced to develop within a few minutes, attained a maximum intensity after 15—20 minutes, and then slowly gave way to an olive-green, which in turn was replaced by a permanent yellow colour. The final solution possessed a faint green fluorescence resembling that often seen in the final stage of the Adamkiewicz reaction. During the course of this study a number of carbolines, derived not only from tryptophan but also from *r*-α-methylamino-β-3-indolylpropionic acid (Miller and Robson, J., 1938, 1910), have been tested with the " reagent " and in all cases the range of colours described above has been obtained. The reaction is exceedingly sensitive.

It will be clear from the foregoing that 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic

acid may be utilised for testing samples of concentrated sulphuric acid for the presence of oxidising agents. Tested in this way, certain samples of sulphuric acid purchased on the market and labelled " commercial " have been found to contain smaller amounts of oxidising agents than others labelled " pure ".

It became of interest, at this stage, especially in view of the bearing which the reaction was considered to have on a problem referred to below, to gain further knowledge regarding the chemical grouping in the molecule of 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid which is responsible for the colour development.

Attempts were first made to isolate the pigment from the sulphuric acid mixture when the blue colour had reached its maximum intensity. When the blue solution was mixed with a large volume of water, the colour quickly disappeared and no solid could be isolated from the resulting yellow mixture. This is contrary to the experience of Fearon (*loc. cit.*), who isolated his blue pigment by such a procedure. The pigment could not be extracted from the mixture by such organic solvents as benzene, light petroleum, chloroform, and carbon disulphide, and decolorisation of the solution took place when sulphur dioxide was bubbled through it, the colour being restored by removing the sulphur dioxide with a current of nitrogen.

Such a mode of attack not offering much hope of success, an investigation was undertaken of the colour, if any, produced by the action of the " reagent " on those compounds which may be considered as forming part, or possessing a structure similar to that, of the molecule of 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid.

Table of compounds tested and their colour reactions with the " reagent."

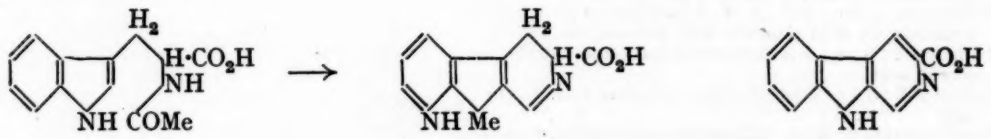
Benzene	Colourless
Proline (Dakin, *J. Biol. Chem.*, 1920, **44**, 499)	,,
Piperidine-2-carboxylic acid (Clemo and Ramage, J., 1931, 437)	,,
7-Hydroxy-1 : 2 : 3 : 4-tetrahydro*iso*quinoline-3-carboxylic acid	,,
Indole	Pale pink (permanent)
6-Methoxyindole (Harvey and Robson, J., 1938, 97)	,, ,, ,,
α-Methylindole (Fischer, *Annalen*, 1886, **236**, 126)	Colourless
β-Methylindole (*idem, ibid.*)	,,
αβ-Dimethylindole (*idem, ibid.*)	,,
Carbazole	Deep green (permanent)
l-Tryptophan (Cole, " Practical Physiological Chemistry," 9th ed., 1933)	Pale pink ⟶ weak purple ⟶ yellow with strong fluorescence
l-Tryptophan methyl ester hydrochloride (Abderhalden and Kempe (*Z. physiol. Chem.*, 1907, **52**, 207)	,, ,, ,, ,, ,,
r-α-Methylamino-β-3-indolylpropionic acid (Miller and Robson, J., 1938, 1910)	,, ,, ,, ,, ,,
Tryptamine hydrochloride (Ewins, J., 1911, **99**, 270)	,, ,, ,, ,, fluorescence less marked
2 : 3 : 4 : 5-Tetrahydro-β-carboline-4-carboxylic acid	" Carboline-blue " colour reaction
2-Methyl-2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid (Harvey and Robson, *loc. cit.*)	,, ,, ,, ,,
8-Methoxy-2-methyl-2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid (Harvey and Robson, *loc. cit.*)	,, ,, ,, ,,
2-Phenyl-2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid	,, ,, ,, ,,
3-*Methyl*-2 : 3 : 4 : 5-*tetrahydro-β-carboline-4-carboxylic acid*	,, ,, ,, ,,
2 : 3-*Dimethyl*-2 : 3 : 4 : 5-*tetrahydro-β-carboline-4-carboxylic acid*	,, ,, ,, ,,
2-*Phenyl*-3-*methyl*-2 : 3 : 4 : 5-*tetrahydro-β-carboline-4-carboxylic acid*	,, ,, ,, ,,
2-*Hydroxymethyl*-2 : 3 : 4 : 5-*tetrahydro-β-carboline-4-carboxylic acid*	Immediate blue, quickly giving way to a deep olive-green, which in turn is gradually replaced by a greenish-yellow fluorescence
2 : 3 : 4 : 5-*Tetrahydro-β-carboline*-2 : 4-*dicarboxylic acid*	Immediate blue tinged with pink, changing to purple, then to brownish-red
Methyl 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylate hydrochloride	" Carboline-blue " colour reaction
Norharman	Yellow solution with conspicuous fluorescence
Harman (Harvey and Robson, *loc. cit.*)	,, ,, ,, ,, ,,
Harmine (Harvey and Robson, *loc. cit.*)	,, ,, ,, ,, ,,

Harmaline hydrochloride	Intense yellow-brown, changing quickly to a permanent clear amber
Tetrahydroharmine (Perkin and Robinson, J., 1919, **115**, 933)	Weak purple, changing quickly to olive-green then to yellow with a green-yellow fluorescence
N-Methyltetrahydroharmine (*idem, ibid.*)	,, ,, ,, ,, ,,
2-Methyl-2 : 3 : 4 : 5-tetrahydro-β-carboline-2-carboxylic acid (Hahn and Werner, *Annalen*, 1935, **520**, 123)	Immediate transient blue, changing to bright green, then shortly to a permanent yellow
2-*m*-Hydroxybenzyl-2 : 3 : 4 : 5-tetrahydro-β-carboline-2-carboxylic acid (*idem, ibid.*)	,, ,, ,, ,, ,,
Norharman-2-carboxylic acid (Kermack, Perkin, and Robinson, J., 1921, 1602)	Yellow fluorescence
Norharman-4-carboxylic acid	,, ,,

Examination of the results tabulated above shows that the precursor of the blue pigment must possess a complex structure. Apart from indole and 6-methoxyindole, which yield a pink coloration, the simple molecules such as benzene, proline, piperidine-2-carboxylic acid, as might be expected, do not yield a colour with the " reagent." With carbazole a permanent deep green colour is obtained. Turning to the β-carboline bases, norharman, harman, and harmine, each gives a yellow solution characterised by a conspicuous fluorescence, and it is only when their molecules are fully hydrogenated in the pyridine ring, as in 2 : 3 : 4 : 5-tetrahydro-β-carboline, that a range of colours approximating to that described above is obtained. With the latter compound, however, the initial colour is purplish and the life period of the colour range considerably shorter than that obtained from 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid. A similar intensification of the colour obtained with the " reagent " following reduction of the compound under examination is seen on passing from norharman-2-carboxylic acid, which yields a yellow fluorescence, to 2-methyl-2 : 3 : 4 : 5-tetrahydro-β-carboline-2-carboxylic acid, which gives rise to a blue coloration, which, however, is not the same as that produced by its isomer, 2-methyl-2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid, in that it is tinged with pink and changes very rapidly to a permanent brownish-red colour.

From such findings, it would seem that, for the production of the range of colours described above, it is essential that the β-carboline nucleus be hydrogenated in positions 2, 3, 4 and 5 and carry a carboxyl group in position 4.

Whilst the exact structure of the blue pigment has not been definitely ascertained, certain indications of its probable nature exist. Norharman-4-carboxylic acid (IV) (King and Stiller, J., 1937, 466)—the second oxidation product of 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid—yields with concentrated sulphuric acid a yellow fluorescence similar to that obtained when the mother substance is treated with the " reagent." The question therefore arises whether the intermediate compound, 4 : 5-dihydro-β-carboline-4-carboxylic acid (III), is the blue pigment. So far, however, all attempts to synthesise a compound (III) of such a structure from acetyltryptophan (II) by ring closure have proved unsuccessful.



(II.) (III.) (IV.)

The Action of Formaldehyde on Tryptophan.

If formaldehyde is added to (*a*) an aqueous acid solution of tryptophan, and the mixture boiled (Jacobs and Craig, *loc. cit.*), (*b*) an aqueous solution of tryptophan buffered at p_H 8·0, and the mixture kept at 38° (Wadsworth and Pangborne, *loc. cit.*), or (*c*) a solution of the sodium salt of tryptophan, and the mixture kept at 38°, the product in each case is 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid, m. p. 306°.

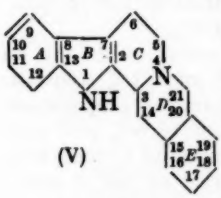
On the other hand, Homer (*Biochem. J.*, 1913, **7**, 101) has shown that, if formaldehyde is allowed to react with a neutral aqueous solution of tryptophan at 38°, a granular crystal-

line substance, m. p. 226—240°, separates after a few hours. Homer assigned to this compound the empirical formula $C_{12}H_{12}O_2N_2,2H_2O$ and showed that it can be changed very readily into a second compound, called by her the " ether oxidation product ", m. p. 324°. Ascribing to the latter compound the formula $C_{24}H_{26}O_5N_4$, she regarded it as a dimethylenetryptophan complex. In our hands the compound, m. p. 226—240°, undergoes the transformation described by Homer, but the product so obtained melts at 306°. It gives the " carboline-blue " colour reaction described above, yields norharman on oxidation with dichromate, and a mixture of it and 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid melts at 306°. The " ether oxidation product " is therefore 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid.

This finding would indicate that the compound, m. p. 226—240°, is α-hydroxymethylamino-β-3-indolylpropionic acid, *i.e.*, the simple addition product of formaldehyde and tryptophan, which substance, crystallising with one molecule of water, would have the formula $C_{12}H_{14}O_3N_2,H_2O$ and not that suggested by Homer. Baker and Happold (*Biochem. J.*, 1940, **34**, 657) state that all their preparations of this substance made according to Homer melt at 196° and that in view of the discrepancies in the analytical figures obtained for their product they doubt " whether the action of formaldehyde on *l*-tryptophan is as simple as the structures assigned by Homer suggest ". Results similar to those of Baker and Happold have been obtained in this laboratory and are due, it is believed, to the presence, in the required product, of 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid, the amount of which increases as the time of incubating the mixture of formaldehyde and tryptophan is extended.

Constitution of Yohimbine, $C_{19}H_{22}N_2(OH)(CO_2Me)$.—Apart from the light that the present work throws on the mechanism of the Adamkiewicz test, it would appear that the colour reactions given by 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid are of particular value with reference to the problem of the constitution of yohimbine.

This alkaloid, whose skeletal structure was shown by Barger and Scholz (*loc. cit.*) and by Hahn, Kappes, and Ludewig (*loc. cit.*) to be as depicted (V), reacts with the " reagent " to yield a range of colours similar in every respect to that given by the 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acids. It would appear, therefore, that the carbomethoxy-group present in the alkaloid is attached to C_5 (cf. footnote, page 153). Such a conclusion conflicts with that of Hahn *et al.* (*loc. cit.*) and of Barger (Thorpe's " Dictionary of Applied Chemistry," Suppl. Vol., 1935, 720), who are of the opinion that the carboxyl group is located at C_{16}. According to this view a suitable starting point for the synthesis of the alkaloid would be tryptophan methyl ester and not tryptophan as suggested by Hahn and Werner (*loc. cit.*). This idea is being pursued practically.



(V)

Experimental.

The " reagent " consists of pure sulphuric acid containing an oxidising agent, *e.g.*, ferric chloride, potassium persulphate, sodium nitrite, nitroprusside, or ferricyanide. Most samples of " commercial " sulphuric acid have been found suitable for the purpose described.

7-Hydroxy-1 : 2 : 3 : 4-tetrahydroisoquinoline-3-carboxylic Acid.—Strict observance of the conditions detailed by Pictet and Spengler (*Ber.*, 1911, **44**, 2030) repeatedly failed to yield this product in a pure form by the action of methylal and concentrated hydrochloric acid on tyrosine. Tests, therefore, were carried out on the amorphous compound obtained.

α-Hydroxymethylamino-β-3-indolylpropionic Acid.—*l*-Tryptophan (0·6 g.) was dissolved in water (12 ml.), formalin (2 ml.) added, and the mixture incubated at 38° for not more than 3—4 hours. The colourless, crystalline, but rather granular solid which had then separated was collected, washed with cold water, and dried in a vacuum. Yield, 60% (Found : N, 11·2; loss after drying at 130°/5 mm. for 4 hours, 13·9. Calc. for $C_{12}H_{14}O_3N_2,2H_2O$: N, 11·1; H_2O, 14·2%).

2 : 3 : 4 : 5-Tetrahydro-β-carboline-4-carboxylic Acid.—This was obtained in three ways. (1) A solution of α-hydroxymethylamino-β-3-indolylpropionic acid in dilute aqueous ammonia was boiled for 30 minutes. The solution was then clarified with charcoal, filtered, and con-

centrated to a small volume. The product separated in colourless leaflets, m. p. 306°. (2) A solution of the above amino-acid in water was boiled for 2 hours, concentrated to a small volume, and allowed to cool. The product, recrystallised from boiling water, had m. p. 306°. (3) *l*-Tryptophan (0·2 g.; 1 mol.) was dissolved in N/10-sodium hydroxide (10 ml.; 1 mol.) containing formalin (0·11 ml.; 1·1 mols.), and the mixture incubated at 38° for 15 hours. When the p_H of the cold solution was adjusted to approximately 6·5 by the addition of N/10-hydrochloric acid, 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid, m. p. 306°, was precipitated. Yield, 80%.

Norharman.—2 : 3 : 4 : 5-Tetrahydro-β-carboline-4-carboxylic acid (0·45 g.) was dissolved in boiling water (250 ml.) and treated with 10% potassium dichromate solution (30 ml.) and glacial acetic acid (6 ml.). The immediate formation of a cloudiness in the solution was followed by the evolution of carbon dioxide. Boiling was continued for about 1½ minutes, the solution then cooled, and the excess of oxidising agent removed by sulphur dioxide. The mixture was rendered alkaline with sodium carbonate solution and extracted five times with ether. The extract was evaporated to dryness, and the residue recrystallised from methyl alcohol, forming long colourless needles, m. p. 200°. Kermack, Perkin, and Robinson (*loc. cit.*) give 198·5°. The yield of the pure product was 50—60% (Found : N, 16·6. Calc. for $C_{11}H_8N_2$: N, 16·6%).

Methyl 2-Methyl-2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylate Hydrochloride.—Absolute methyl alcohol (5 ml.) in which was suspended 2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic acid (0·25 g.) was saturated with hydrogen chloride; after a few minutes the ester hydrochloride separated in long colourless needles. After some 15 minutes the product was collected, sucked dry, washed with a few drops of cold ethyl acetate, and dried over sulphuric acid (yield, quantitative). It melted at 264° (decomp.) and was extremely soluble in alcohol and water, but less so in ethyl acetate and ether (Found : N, 10·0. $C_{14}H_{16}O_2N_2$,HCl requires N, 10·0%).

2-Hydroxymethyl-2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic Acid.—*l*-Tryptophan (0·5 g.) was dissolved in 0·1N-sulphuric acid (24·5 ml.; 1 mol.), the diethylacetal of glycollaldehyde (0·35 g.; 1·1 mols.) added, and the mixture heated in a corked vessel in a boiling water-bath for 4 hours. The solution was then clarified with charcoal, treated with aqueous ammonia to bring its p_H to about 6·0, and evaporated to a small bulk on the water-bath. The pale pink crystals which gradually separated were recrystallised from water, forming long colourless needles possessing a steel-grey sheen, m. p. 234° (Found for a specimen dried at 120°/2 mm. : C, 63·2; H, 5·8; N, 11·25. $C_{13}H_{14}O_3N_2$ requires C, 63·4; H, 5·7; N, 11·4%).

2 : 3 : 4 : 5-Tetrahydro-β-carboline-2 : 4-dicarboxylic Acid.—To *l*-tryptophan (0·5 g.) in N/10-sulphuric acid (24·5 ml.; 1 mol.) was added glyoxylic acid (25 ml. of a 1% solution; 1·4 mols.), the mixture being subjected to the treatment described in the previous preparation. When the solution, separated from a reddish tar, was concentrated to about 10 ml., pale pink crystals (0·37 g.; 50% yield) were obtained. Once recrystallised, the compound formed thin, colourless rhomboids, m. p. *ca.* 270° (decomp.) (Found for a specimen dried at 120°/2 mm. : C, 59·7; H, 4·8; N, 10·75. $C_{13}H_{12}O_4N_2$ requires C, 60·0 : H, 4·6; N, 10·76%).

3-Methyl-2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic Acid.—To a cool solution of *r*-α-methylamino-β-3-indolylpropionic acid (0·5 g.) in water (75 ml.), a slight excess (0·4 ml.; 2·3 mols.) of commercial formalin was added, and the whole incubated at 38° for 15 hours. The " solid " which separated was collected (0·11 g.), and the filtrate concentrated to a small volume on the boiling water-bath. The bundles of stout rods which settled on cooling were collected, washed with absolute alcohol, and dried in a desiccator. Concentration of the mother-liquor gave a further crop of the *carboline-carboxylic acid.* Yield, 0·40 g. (76%). On recrystallisation from water the carboline was obtained in bundles of fine rods, m. p. 208° after softening at 194° (Found for a sample dried at 130°/4 mm. : N, 11·3. $C_{13}H_{14}O_2N_2,H_2O$ requires N, 11·3%).

The " solid," recrystallised from dilute aqueous ammonia, formed sheaves of colourless needles, m. p. above 340°. With " commercial " sulphuric acid it gave a fine permanent purple colour, indicating that its structure is not the same as that of the carbolinecarboxylic acid. It is receiving further investigation.

2 : 3-Dimethyl-2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic Acid.—A solution consisting of *r*-α-methylamino-β-3-indolylpropionic acid (0·5 g.) in N/2-hydrochloric acid (4·6 ml.; 1 mol.) and freshly distilled acetaldehyde (0·19 ml.; 1·5 mols.) was incubated overnight, neutralised with the required amount (2·3 ml.) of N-sodium hydroxide, and left to crystallise. The colourless rods were collected, washed with a little cold water, then with absolute alcohol, and dried in a desiccator. Concentration of the mother-liquor gave a further small crop. Total yield, 0·51 g. (90%). The product melted at 243—245° (Found : N, 11·4. $C_{14}H_{16}O_2N_2$ requires N, 11·5%).

2-Phenyl-3-methyl-2 : 3 : 4 : 5-tetrahydro-β-carboline-4-carboxylic Acid.—No trace of carboline could be detected on incubating for 10 days a neutral or slightly acid solution of the reactants mentioned below. When 1 mol. of acid was used, a minute yield of carboline was obtained after a similar period of time. The compound was finally prepared after the method of Jacobs and Craig (*loc. cit.*). γ-α-Methylamino-β-3-indolylpropionic acid (0·3 g.) together with N-sulphuric acid (1·5 ml.; 1 mol.) and benzaldehyde (1·5 ml.; 10 mols.) in 75% aqueous alcohol (3 ml.) was refluxed for 20 hours on the boiling water-bath. Excess of aqueous ammonia was added to the cooled solution, and the free benzaldehyde removed with ether. When the aqueous solution was clarified with charcoal and concentrated, typical rod-like crystals of the *carboline-carboxylic acid* settled in 70% yield. After a further recrystallisation from water the pure product melted, on slow heating, at 219° (sharp) (Found: N, 8·7. $C_{19}H_{18}O_2N_2,H_2O$ requires N, 8·65%).

We desire to express our thanks to Dr. H. King for a sample of norharman-4-carboxylic acid (King and Stiller, *loc. cit.*). Part of the work herein described was done during the tenure by one of us (E. J. M.) of a Berridge Studentship awarded by the Delegacy of the University of London, King's College.

UNIVERSITY OF LONDON, KING'S COLLEGE. [*Received, November 25th*, 1940.]

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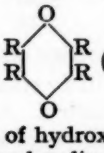
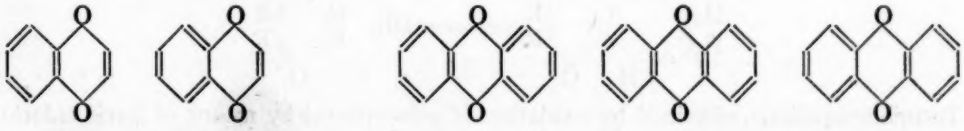
35. *Absorption Spectra in Relation to Quinones: 1 : 4-Naphthaquinone, Anthraquinone, and Their Derivatives.*

By R. ALAN MORTON and W. TREVOR EARLAM.

The spectra of 1 : 4-naphthaquinone and its alkyl substitution products are accounted for by the summation of effects due to (*a*) $C_6H_4<^{CO\cdot R}$ ($\lambda\lambda_{max.}$ 2500 and 3300 A.) and (*b*)  ($\lambda\lambda_{max.}$ 2620, 2720 A. quinonoid, and $\lambda_{max.}$ *ca.* 4000 A. carbonyl). The spectra of hydroxy-derivatives reflect similar summations, complicated somewhat by hydrogen bonding in α-hydroxy-compounds.

The spectrum of anthraquinone is reproduced closely by $2a + b$. In the hydroxyanthraquinones, the two bands ascribed to *a* can vary independently, as also can the quinonoid and carbonyl bands of *b*. α-Substitution, with its concomitant hydrogen bonding, favours fixation of Kekulé forms so as to diminish the quinonoid element in *b* and enhance the importance of the carbonyl aspect. This tendency is reversed in β-substitution products.

1 : 4-NAPHTHAQUINONE and anthraquinone possess, in terms of resonance, hybrid structures, the extreme forms being:



Apart from the C·C:O single bonds, all the carbon–carbon linkages possess some degree of double-bond character, and a knowledge of the precise electron-density distribution might well afford a basis for predicting many properties. Such knowledge is not easily gained, but some advance is possible by the careful interpretation of absorption spectra.

Morton and Stubbs (J., 1940, 1347) have shown that salicylaldehyde and *o*-hydroxyacetophenone are spectroscopically similar, having maxima near 3250 A., log ε 3·5, and 2550 A., log ε 4·0, characteristic of the benzenoid chromophore $C_6H_4<^{CO\cdot R}$. Klingstedt (*Compt. rend.*, 1923, **176**, 1550), Light (*Z. physikal. Chem.*, 1926, **122**, 414), and Scheibe (*Ber.*,

1926, **59**, 2617) have shown that simple quinones, *e.g.*, 1 : 4-benzoquinone, show: (i) resolved absorption in the visible region with low ε values (1—20), (ii) a marked inflexion at 2800—2900 A. of moderate intensity, log ε *ca.* 2·5, and (iii) an intense band, $\lambda_{max.}$ 2410 A., log ε 4·30. In *p*-xyloquinone the absorption is similar, but the 2410 A. maximum is displaced to 2500 A.

Macbeth, Price, and Winzor (J., 1935, 325) found that 1 : 4-naphthaquinone shows a marked inflexion at 3900—4600 A., log ε 1·9—1·6, a well-defined band at $\lambda_{max.}$ 3340 A., log ε 3·44, an inflexion at 2560 A., log ε 4·13, and a sharp maximum at 2460 A., log ε 4·28 (solvent, alcohol). Our data for hexane solutions are shown in Table I. Introduction of alkyl groups has interesting effects which have been important in recent work on the *K* vitamins. Webb (see Fieser *et al.*, *J. Amer. Chem. Soc.*, 1939, **61**, 1927) and Ewing, Vandenbelt, and Kamm (*J. Biol. Chem.*, 1939, **131**, 352), in extending the work of several groups of investigators, recorded four maxima in the region 2400—2800 A. for disubstituted products.

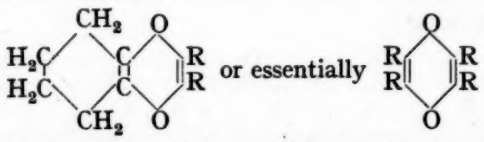
TABLE I.

	$\lambda_{max.}$, A.	log $\epsilon_{max.}$		$\lambda_{max.}$, A.	log $\epsilon_{max.}$
1 : 4-Naphthaquinone (Fig. 1)	2410	4·32	2-3 : Dimethyl-1 : 4-naphthaquinone	2430	4·26
	2460	4·37		2490	4·26
	2510	4·28		2600	4·28
	2560	4·12		2690	4·28
	3300	3·44		3300	3·38
2-Methyl-1 : 4-naphthaquinone	2440	4·29	Vitamin-K_1	2430	4·37
	2500	4·29		2490	4·39
	2630	4·30		2600	4·38
	3340	3·38		2700	4·36
				3250	3·52
2-Ethyl-1 : 4-naphthaquinone	2450	4·31	Vitamin-K_2	2430	4·20
	2500	4·34		2490	4·24
	2550	4·33		2600	4·18
	2670	4·26		2700	4·18
	3300	3·4		3250	3·45

It is clear from the work of Macbeth *et al.* (*loc. cit.*) that an inflexion 4000—4500 A., log ε < 2, is also common to substances of this type, but many workers omit to study solutions sufficiently concentrated for the absorption in this region to be recorded. Ewing *et al.* confirmed earlier observations on the spectra of certain reduction products of vitamins-K_1 and -K_2, and concluded that when the quinonoid part of the molecules was retained, only the maxima at 2600 and 2700 A. persisted (measurements at 4000—4500 A. were apparently not feasible):

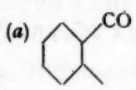
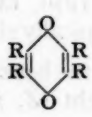
	Reduced vitamin-K_1 ($C_{31}H_{50}O_2$).	Reduced vitamin-K_2 ($C_{40}H_{60}O_2$).
$\lambda_{max.}$, A.	*ca.* 2600, 2700	2600, 2700
log $\epsilon_{max.}$	4·23	4·12

The absorptive part of both substances is

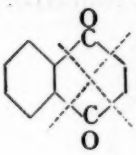


α-Tocopherylquinone, obtained by oxidation of α-tocopherol by means of ferric chloride, contains the same chromophoric grouping and shows λ$\lambda_{max.}$ 2625 and 2725 A., log ε 4·23 (Karrer and Geiger, *Helv. Chim. Acta*, 1940, **23**, 455).

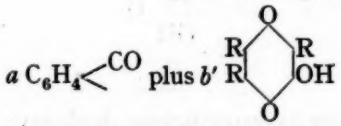
The substituted 1 : 4-naphthaquinones (Table I) thus exhibit spectra little different from the simple summation *a* + *b*:

(*a*) 	$\lambda_{max.}$, A.	log $\epsilon_{max.}$	(*b*) 	$\lambda_{max.}$, A.	log $\epsilon_{max.}$
	2430	4·02		*ca.* 2600	*ca.* 4·2
	2495	4·025		2706	
	3290	3·63		~4000—4500	*ca.* 2·0

Chromophore *a* is potentially perhaps capable of functioning twice (see inset), but from the ε values only appears to count once.



The foregoing interpretation may be extended to the hydroxynaphthaquinones studied by Macbeth, Price, and Winzor (*loc. cit.*). Our data on naphthazarin are in good agreement. The figures in Table II, with those of Cooke, Macbeth, and Winzor (J., 1939, 878), lead to the view that the structure (I) (present also in lapachol, lomatiol, *iso*lomatiol, dihydroxyhydrolapachol, α-lapachone, and phthiocol) can be regarded chromophorically as



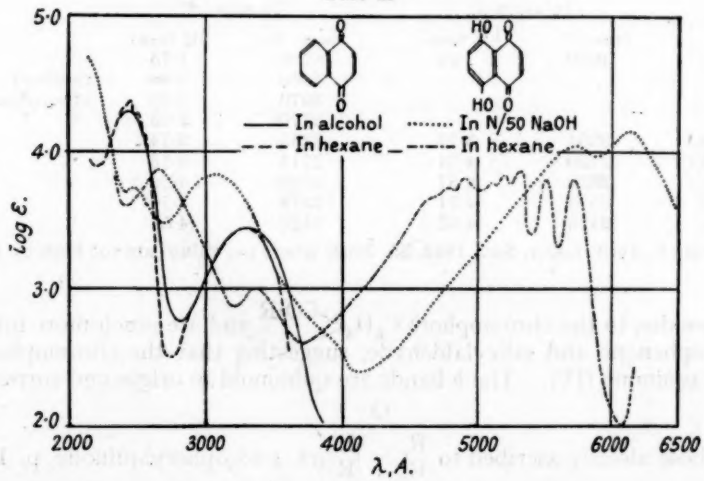
a plus *b'*; *a* has the usual maxima whilst *b'* has the quinonoid absorption at 2600—2700 A. displaced to *ca.* 2800 A., log $\epsilon_{max.}$ 4·2, and the carbonyl absorption at 3900—4500 A. increased in intensity from log ε 2 to 3, *i.e.*, about tenfold. Such an increase in ε also follows the introduction of hydroxyl into benzene (cf. Morton and Stubbs, *loc. cit.*). The counteracting effect of acetylation is common to both the benzenoid and the quinonoid chromophore.

TABLE II.

	$\lambda_{max.}$, A.	log $\epsilon_{max.}$			$\lambda_{max.}$, A.	log $\epsilon_{max.}$	
2-Hydroxy-1 : 4-naphthaquinone (lawsone)	2440	4·20	*a*	5 : 8-Dihydroxy-1 : 4-naphthaquinone (naphthazarin) (Fig. 1)	2470	3·73	*a*
	2760	4·20	*b*		2540	3·84	*a*
	3310	3·45	*a*		2700	3·92	
	~3950	3·30			2840	3·84	*b*
	4600	2·0	*b*		2980	3·52	
2 : 3-Dihydroxy-1 : 4-naphthaquinone (*iso*naphthazarin)	2700	4·12	*b*		3380	2·95	*a*
	2820	4·05	*b*		4500	3·50	
	3350	3·31	*a*		4850	3·75	
	4450	3·26	*b*		5130	3·85	*b*
	~3900—5100				5620	3·60	
5-Hydroxy-1 : 4-naphthaquinone (juglone)	2490	4·12	*a*		6250	2·92	
	2620	4·00	*b*				
	3390	3·18	*a*				
	4250	3·6					
	~4950	2·8	*b*				

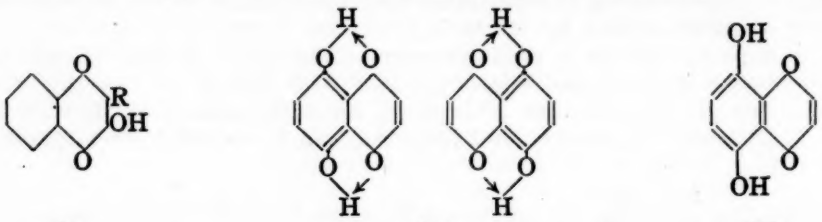
~ denotes inflexion.

FIG. 1.



In juglone (Macbeth, Price, and Winzor, J., 1935, 325) chromophore *a* appears with somewhat diminished intensity, and the long-wave absorption of the quinonoid chromophore is displaced to 4250 A., log ε *ca.* 3·6. In naphthazarin the benzenoid absorption is weakened still more, whilst the quinonoid absorption at 2600—2700 A. is displaced some-

what and that at 3900—4500 A. is displaced considerably. Resonance here involves the extremes (II) and (III), and hydrogen bonding favours fixation of (II) rather than (III).



(I.) (II.) (III.)

The data of Lugg, Macbeth, and Winzor (J., 1937, 1039) on hydroxyjuglone, hydroxydroserone, naphthapurpurin, and their acetates show clearly how acetylation restores a normal benzenoid absorption: $\lambda\lambda_{max.}$ 3450—3500, 2500—2600 A., log $\varepsilon_{max.}$ 3·4—3·5 and *ca.* 4·0 respectively. In these acetates the quinonoid contribution to the observed absorption is of minor significance.

1 : 2-Naphthaquinones show spectra capable of similar interpretation. Goldschmidt and Graef (*Ber.*, 1928, **61**, 1858) studied the parent substance, and Macbeth, Price, and Winzor (*loc. cit.*) the 4-methoxy-derivative. Later (J., 1939, 878) Cooke, Macbeth, and Winzor discussed a series of 1 : 2-naphthaquinones from natural products. From these studies the *a* bands at 2500—2600, log ε 4·35—4·5, and *ca.* 3330 A., log ε *ca.* 3·2, are easily recognised. An inflexion near 2700—2860 A., log ε 3·8—4·0, is less intense than the absorption of 1 : 4-naphthaquinones in the same region, but selective absorption at 4000—4200 A. is well marked and more intense (log ε 3·3—3·4 as compared with log ε *ca.* 2) than that of the 1 : 4 analogues. It is sometimes possible to record weak selective absorption near 5000 A., log ε 2·0; this is obviously carbonyl absorption. The 1 : 2-naphthaquinones do not exhibit the well-resolved absorption in the region 2700—2800 A. characteristic of the ethenoid linkages in the quinonoid chromophore of 1 : 4-quinones.

The spectrum of anthraquinone (Table III, Fig. 2) can now be accounted for readily.

TABLE III.

Anthraquinone.

	In alcohol.		In ether.*		
	$\lambda_{max.}$, A.	log $\epsilon_{max.}$	$\lambda_{max.}$, A.	log $\epsilon_{max.}$	
b	4050	1·95	4200	1·75	
			4060	1·88	resolved
			3970	1·95	absorption
			3770	2·05	
a	3255	3·75	3235	3·74	
b	2720	4·31	2715	4·18	
b	2628	4·31	2630	4·22	
a	2525	4·71	2515	4·70	
a	2435	4·52	2420	4·51	

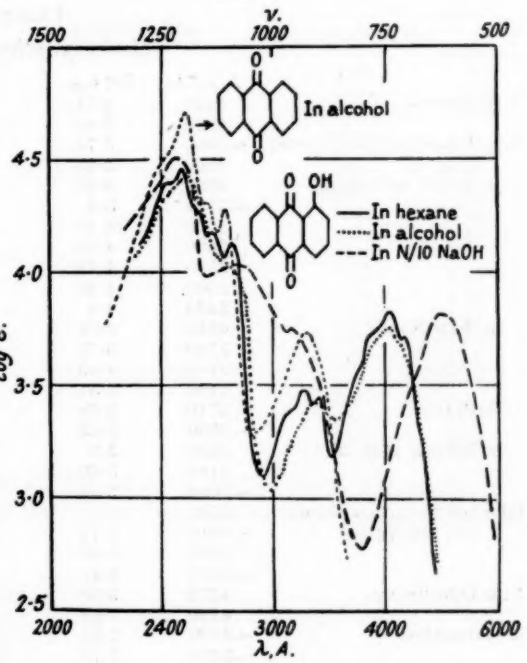
* Cf. Anderson (*J. Amer. Chem. Soc.*, 1933, **55**, 2094) where log values are too high by 1·0 throughout the spectrum.

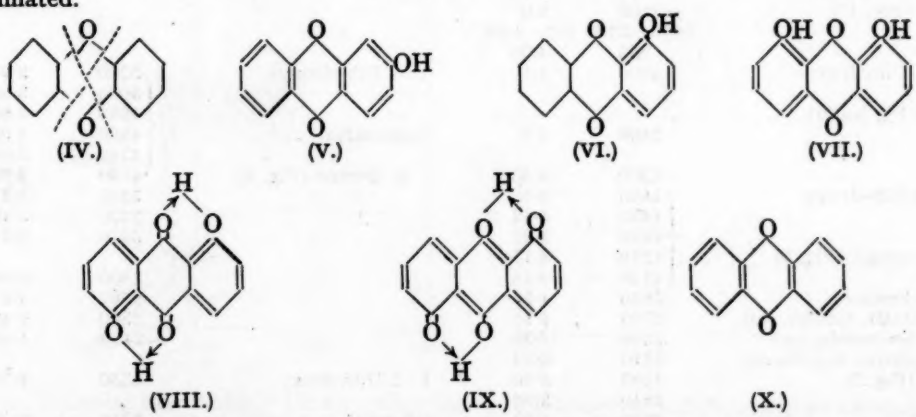
The *a* bands are due to the chromophore $C_6H_4<^{CO\cdot R}$ and are much more intense than in *o*-hydroxyacetophenone and salicylaldehyde, suggesting that the chromophore functions twice in anthraquinone (IV). The *b* bands are quinonoid in origin and correspond almost exactly with those already ascribed to (cf. α-tocopherylquinone, p. 160).

Introduction of hydroxyl groups into anthraquinone produces considerable effects which vary with the position and number of substituents. It will be convenient to note first a group of distinct effects: (i) Displacement of maxima in the direction of longer

wave-lengths without influencing the probability of the relevant electronic process, *i.e.*, no change in $\varepsilon_{max.}$; (ii) marked increase or decrease in $\varepsilon_{max.}$ not accompanied by wave-length displacements; (iii) an alteration in the relative importance of the benzenoid and the quinonoid contributions to the absorption exerted by the resonance hybrid. In all cases hydroxyl groups bring about an increase in the absorption shown by anthraquinone near 4050 A., log ε *ca.* 2; this increase is least (log ε 3·15—3·55) for β-substituted products and greatest for αα'- (1 : 4-; 1 : 8-; 1 : 5-) derivatives, whilst 1- and 1 : 2-derivatives occupy an intermediate place. This absorption is attributed to the carbonyl group within the quinonoid chromophore. The wave-length displacements vary in the same sense, and, in fact, the β-substituted products differ little from the parent substance in this respect. The anthraquinone maxima at 2628 and 2720 A., log ε 4·31, are likewise due to the quinonoid factor; intensities of absorption for these bands show decreases in 1-, 1 : 5-, 1 : 8-, and 1 : 4-derivatives, and increases in 2- and 2 : 6-derivatives, whereas the two tendencies practically cancel out in alizarin. These effects are the reverse of those occurring at longer wave-lengths (> 4050 A.). The latter absorption in anthraquinone is analogous to the low-intensity long-wave absorption shown by 1 : 4-benzoquinone and 1 : 4-naphthaquinone and must concern an electronic process located in the carbonyl group. On the other hand, the 2628 and 2720 A. maxima of anthraquinone owe their appearance to the –C:C– link in the quinonoid chromophore. On this basis the quinonoid element in the absorption spectrum becomes more important in β- and less important in α-hydroxyanthraquinones, implying some degree of fixation of Kekulé forms (V), (VI), and (VII). It is interesting that if chelation occurs as a result of hydrogen bonding, the resulting resonance, *e.g.*, (VIII) and (IX), requires a weakening of quinonoid character, in so far as (X) tends to be eliminated.

FIG. 2.





The benzenoid element in the spectrum of anthraquinone ($\lambda_{max.}$ 3250 A., log ε 3·75; 2525 A., log ε 4·71) reappears in the hydroxy-derivatives. In 1-hydroxy- and 1-methoxy-

anthraquinone the maxima are little displaced but intensities are roughly halved; 2-hydroxyanthraquinone shows the 3300 A. maximum at log ε 3·55, approximately the intensity at which it occurs in *o*-hydroxyacetophenone, whereas the short-wave maximum (2410 A., log ε 4·31) is twice as intense as the corresponding band. It is therefore to be concluded that as a result of substitution the two benzenoid maxima can vary independently of one another. The 1 : 2-derivatives listed in Table IV show practically undisplaced

TABLE IV.

Hydroxyanthraquinones.

	$\lambda_{max.}$, A.	log $\epsilon_{max.}$		$\lambda_{max.}$, A.	log $\epsilon_{max.}$
1-Hydroxy-	4230	3·71	2-Hydroxy-	3780	3·55
	4060	3·83	in EtOH		
(erythroxyanthraquinone)	~3860	3·74	(Fig. 3)	3300	3·55
(Fig. 2)	3350	3·45		2830	4·46
in EtOH or hexane	3220	3·48		2710	4·55
	~3120	3·4			
	2760	4·13		2410	4·31
	2660	4·18			
	~2560	4·28			
	2500	4·46			
	2435	4·4			
in 0·1N-NaOH	4840	3·82			
	3150	3·75			
	2780	4·03			
	2480	4·51			
1-Methoxy-	3710	3·68	2-Methoxy-	3660	3·45
	~3590	3·63	(Fig. 3)		
in hexane (Fig. 3)	3300	3·5		3300	3·54
	3180	3·49			
	~3050	3·39		2810	4·38
(alcoholic solution shows	2705	4·1		2690	4·54
less resolution)	~2610	4·17			
	2500	4·49		~2300—2500	4·0—4·2
	~2460	4·42			
1 : 5-Dihydroxy-	4370	3·98	2 : 6-Dihydroxy-	~3850	3·35
	4180	3·98		3490	3·90
(anthrarufin)	~3970	3·81	(anthraflavin)	3015	4·28
	~3300	2·75	(Fig. 5)	2742	4·53
in EtOH	2870	3·98		~2650	4·38
	2760	3·98			
	2530	4·24			
	2250	4·57			
1-Hydroxy-5-methoxy-	4000	3·89	2 : 6-Dimethoxy-	3850	3·15
	~3220	3·05	(Fig. 5)	3460	3·87
in EtOH	~2800	3·9		2990	4·35
	2540	4·26		2715	4·55
	2230	4·53		2630	4·40
1 : 5-Dimethoxy-	3870	3·98			
(Fig. 10)	~3200	3·0			
	2650—2760	4·2—4·08			
	255	4·39			
1 : 5-Dihydroxy-	4800	4·1	1 : 4-Dihydroxy-	5200	3·942
				5075	3·942
in 1% NaOH				4980	3·95
	2800	4·2	(quinizarin)	4860	4·02
				4740	3·99
	2300	4·55	in hexane (Fig. 6)	4590	3·95
1 : 8-Dihydroxy-	4565	4·1		3355	3·27
	4455	4·14		3250	3·40
	4315	4·22		2910	3·34
(chrysazin) (Fig. 7)	4210	4·17			
	4110	4·16		2800	4·06
in hexane	2840	4·24		2567	4·23
(in EtOH, similar, but	2740	4·15		2500	4·46
less resolution)	2540	4·36		~2450	4·43
1-Hydroxy-8-methoxy-	4310	3·84			
(Fig. 7)	4100	3·90	1 : 2-Dihydroxy-	4350	3·79
	2810	3·96			
	~2700	4·02	(alizarin)	3310	3·55
	2550	4·24	in EtOH (Fig. 8)	2800	4·3
				2510	4·5

TABLE IV (*contd.*).

	$\lambda_{max.}$, A.	log $\epsilon_{max.}$
1 : 8-Dimethoxy (Fig. 7) very similar to 1 : 5-dimethoxy, but 3200 rather more pronounced.		
1 : 2-Dimethoxy- (Fig. 8)	3740	3·71
	~3300	3·5
	~2800	4·28
	~2700	4·3
	2510	4·46
1 : 2-Dihydroxy-	6075	4·15
	5640	4·22
in 1% NaOH (Fig. 8)		
	273·5	4·52
	229	4·25
1-Hydroxy-2-methoxy-	4410	3·80
	4250	3·83
	3270	3·54
	2790	4·14
in EtOH (Fig. 9)	~2600	
	2545	4·46
	2465	4·53
	2310	4·30
in hexane	4780	3·25
	4495	3·71
	4250	3·83
	4045	3·73
	~3580	3·14
	3300	3·45
	3210	3·49
	~2960	3·7
	2790	4·17
	2690	4·18
	2620	4·31
	2460	4·54
	~2330	4·33
in 1% NaOH	5130	3·83
	3200	3·78
	2850	4·03
	2560	4·54

absorption at 3300 A., log ϵ 3·5, and *ca.* 2500 A., log ϵ 4·5; 1 : 4-dihydroxyanthraquinone, which is similar in that it possesses one unsubstituted ring, also exhibits $\lambda\lambda_{max.}$ 3250 and

FIG. 3.

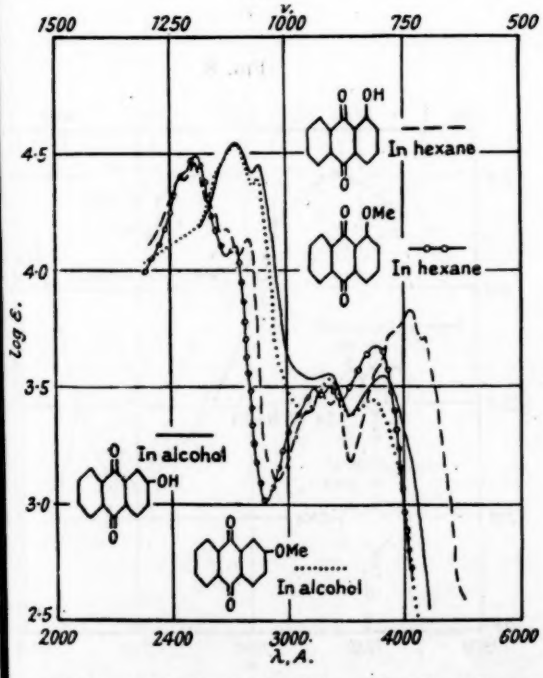
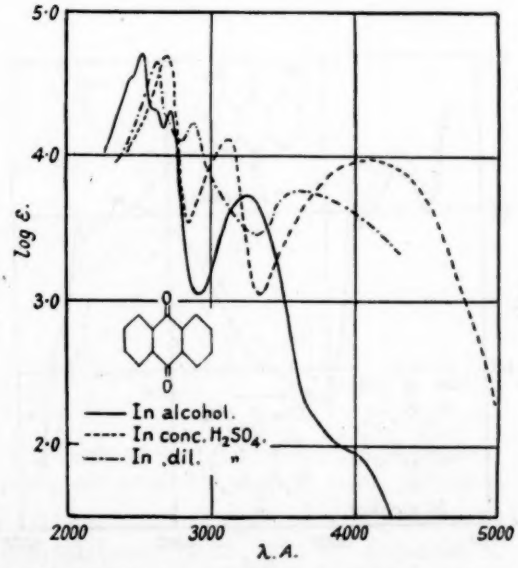


FIG. 4.



2500 A. at similar intensities. On the other hand, 1 : 5-dihydroxyanthraquinone shows the 3300 A. maximum undisplaced but very appreciably reduced in both intensity and persistence, whilst the 2500 A. maximum is also less intense. The 1 : 8-derivatives show no

selective absorption at 3300 A. but the 2500 A. band remains at log $\varepsilon_{max.}$ 4·3. In all the above instances wave-length displacements are small, but in 2 : 6-dihydroxyanthraquinone

FIG. 5.

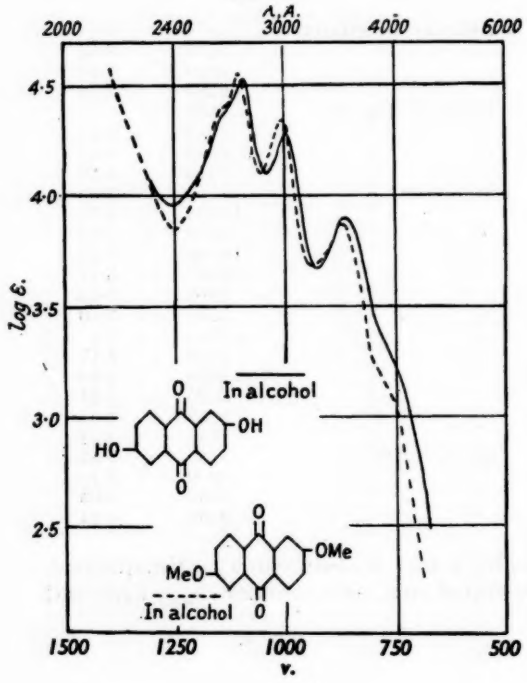


FIG. 6.

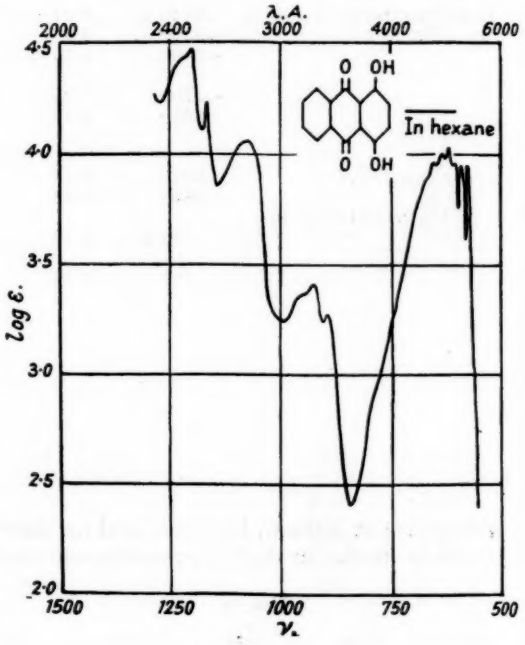


FIG. 7.

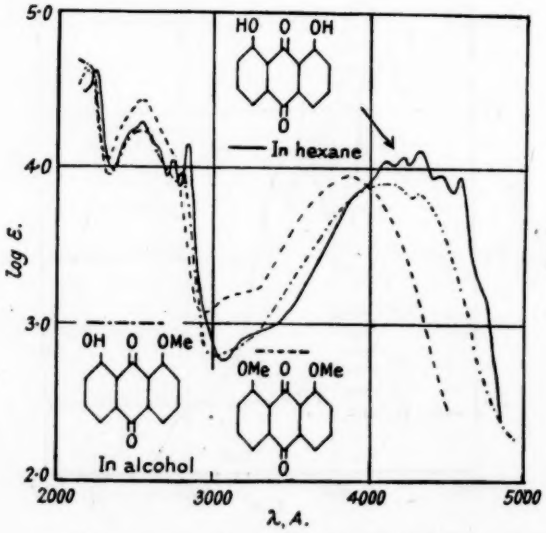
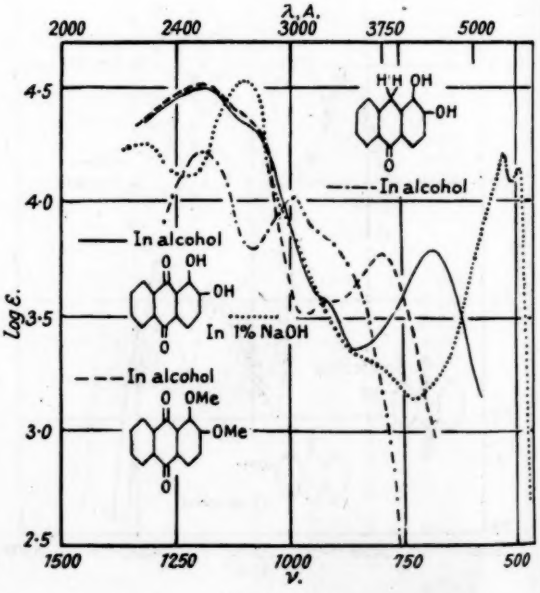


FIG. 8.



the 3250 band is moved to 3490 A., with log ε raised to 3·9; the 2500 A. band is also displaced but lacks persistence.

Although it would be unwise to stress the absolute intensities of absorption in the extreme ultra-violet (because the effects of different chromophores overlap), yet the changes are qualitatively easy to recognise.

FIG. 9.

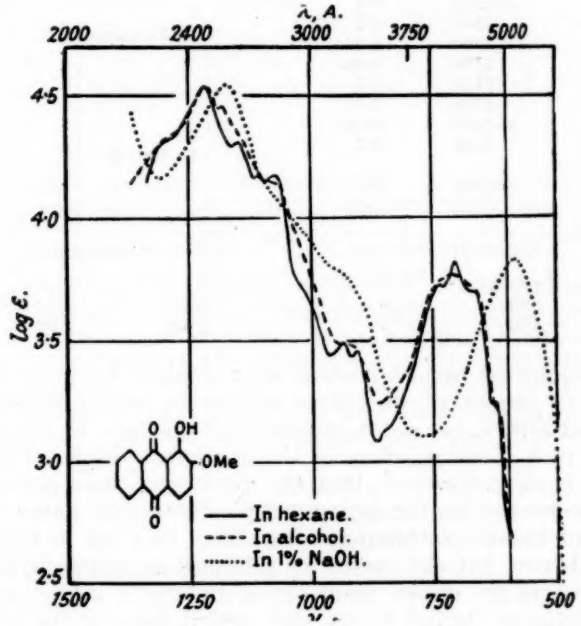
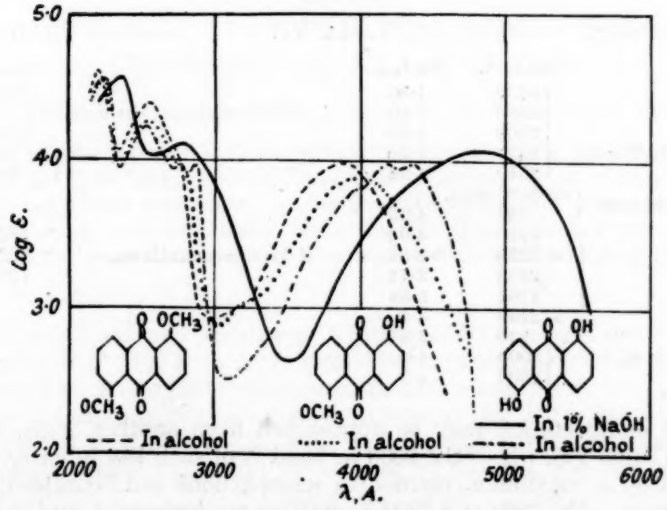
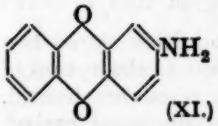


FIG. 10.



Lauer and Horio (*J. pr. Chem.*, 1936, **145**, 279) have studied the aminoanthraquinones; the data in Table V, being obtained by reading their published curves, are approximate. The *a* bands of $C_6H_4<^{CO}$ are shown in both cases, but the quinonoid bands (2628, 2725 A., displaced to 2750—3000 A.) are very much stronger in the β-derivative, again indicating that substitution in the 2-position tends to fix a Kekulé form (XI) with the 1 : 2 link having a predominantly double-bond character.



(XI.)

TABLE V.

1-Aminoanthraquinone.

		$\lambda_{max.}$, A.	log $\epsilon_{max.}$
In hexane		4450	3·75
		~4250	3·6
	a	3300	3·2
		2950	3·65
		2750	4·05
	a	2450	4·6
In EtOH		4700	3·78
		~4100	3·05
	a	3250	3·7
		~2920	3·7
		2850	4·05

2-Aminoanthraquinone.

		$\lambda_{max.}$, A.	log $\epsilon_{max.}$
In hexane		4300	3·4
		4050	3·57
	a	3250	3·80
		2870	4·50
	a	2350	4·6
In EtOH		4300	3·6
		3950	3·25
	a	3300	4·0
		~3180	3·85
	a	2970	4·3
	a	2450	4·5

1-Nitroanthraquinone.

$\lambda_{max.}$, A.	log $\epsilon_{max.}$
3250	3·63
2550	4·57

2-Nitroanthraquinone.

$\lambda_{max.}$, A.	log $\epsilon_{max.}$
3230	3·74
2605	4·60

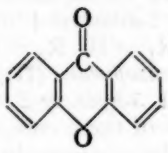
The nitroanthraquinones (data for which were obtained for us by Mr. Z. Sawires) are both very similar in respect of absorption spectra to anthraquinone. The quinonoid maxima at 2620 and 2730 A. are not detectable, but this may be due (particularly in the 2-nitro-derivative) to a masking effect of the somewhat displaced band in the region 2500—2600 A. It is clear, however, that the nitro-group does not enhance the visible absorption in the same way as the amino-group. Horio and Lauer (*loc. cit.*) have also studied a number of hydroxyanthraquinones. Their data are in fairly good agreement with those recorded here, but the curves for solutions in sodium hydroxide and in concentrated sulphuric acid are drawn upside-down and the ε values are meaningless. In addition to the substances studied by us, they record data for the longest wave-lengths of maximum absorption in 2 : 3-, 2 : 6-, 2 : 7-, 1 : 3-, and 1 : 6-dihydroxyanthraquinones.

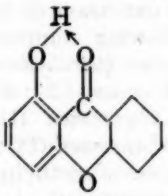
TABLE VI.

	$\lambda_{max.}$, A.	log $\epsilon_{max.}$
Benzophenone	3330	1·85
	2860	2·90
	2500	4·30
2-Hydroxy-5-methylbenzophenone	3420	3·20
	2510	4·04
p-Methoxybenzophenone	no 3420 max.	
	250	4·05
Xanthone	3350	4·02
	a 3226	3·84
	2833	3·73
	2762	3·58
	a 2469	4·4
Deoxyalizarin (Fig. 8)	330	3·8
	3000	4·0
	2500	4·2
o-Methoxybenzophenone	3420	3·20
	2510	4·04
m- ,, ,,	*no* 3420 max.	
	2560	4·05
1-Hydroxyxanthone	3640	3·56
	3390	3·36
	2500	4·28

The task of interpretation may be approached from another angle, beginning with benzophenone (Table VI), where the 3330 A. band is of such low intensity that it can be related to the 3280 A. maximum common to acetophenone and benzaldehyde and due to the carbonyl group. The 2860 and 2500 A. maxima are benzenoid, and in the *o*-hydroxy- and -methoxy-derivatives the former is displaced to 3420 A., *i.e.*, rather further than in salicylaldehyde and *o*-hydroxyacetophenone. Xanthone is interesting in that it shows the maxima already noted as characteristic of $C_6H_4<^{CO}$ (*a*) and in addition shows two maxima, 2833 and 2762 A., which are much more intense than the 2860 A. absorption of benzophenone. If the form (XII) plays any considerable part in the resonance hybrid, these two bands might well correspond with the quinonoid maxima discussed earlier. Some support is given to this suggestion by the absence of the bands from the spectrum

of 1-hydroxyxanthone. This compound, with its tendency towards hydrogen bonding (XIII), would be less markedly quinonoid.

(XII.) 

 (XIII.)

Deoxyalizarin exhibits selective absorption made up of the $C_6H_4<^{CO}$ *a* spectrum, superimposed upon a well-defined band with $\lambda_{max.}$ *ca.* 3000 A.; this is not resolved into two components, and more than one explanation of its origin could be advanced.

The spectroscopic data were obtained by using Hilger E_3 instruments with sectorphotometers. In one arrangement a long-focus sectorphotometer was used in conjunction with a D.C. arc between electrodes of iron and nickel, and in another, a short-focus sectorphotometer with a high-tension (Tesla) spark between tungsten electrodes under water. The latter source gives a continuous spectrum.

All the compounds were carefully purified but the methods used are not described in detail since they were rarely new, and in no case resulted in new criteria of purity.

The authors are indebted to Messrs. A. Hassan and Z. Sawires for some of the measurements, and to the Medical Research Council for a grant which permitted Mr. R. H. Creed to render assistance. They also wish to thank Imperial Chemical Industries (Dyestuffs Group) for the gift of a number of specimens and for other help.

UNIVERSITY OF LIVERPOOL. [*Received, December 23rd,* 1940.]

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36. Cannabis Indica. *Part VII. The Relation between Chemical Constitution and Hashish Activity.*

By P. B. RUSSELL, A. R. TODD, S. WILKINSON, A. D. MACDONALD, and G. WOOLFE.

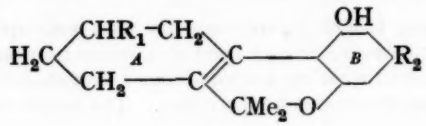
In view of the hashish activity shown by the synthetic tetrahydrocannabinol (I; $R_1 = Me$, $R_2 = C_5H_{11}$) in dogs and rabbits a number of structurally related compounds have been synthesised by the general method previously described (Part IV; J., 1940, 1121) and tested pharmacologically. The bearing of the results so far obtained on the general question of chemical constitution and hashish activity is discussed.

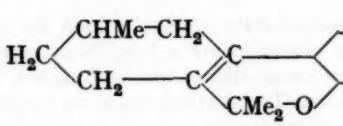
IN Part IV (Ghosh, Todd, and Wilkinson, J., 1940, 1121) a general method was described for the synthesis of 3′ : 4′ : 5′ : 6′-tetrahydrodibenzopyran derivatives by the action of Grignard reagents on 3 : 4-*cyclo*hexenocoumarins and a number of such compounds were thus synthesised, including the tetrahydrocannabinol (I; $R_1 = Me$, $R_2 = C_5H_{11}$). As has been mentioned in Part VI (this vol., p. 137), the latter substance shows hashish activity in rabbits (Gayer test), and its activity in the dog test has been recorded by Adams, Loewe, Pease, Cain, Wearn, Baker, and Wolff (*J. Amer. Chem. Soc.*, 1940, **62**, 2566), who synthesised it independently by a very similar method. It was clearly a matter of great interest to examine a series of compounds related to (I; $R_1 = Me$, $R_2 = C_5H_{11}$) in the hope of ascertaining the structural features essential to the exhibition of hashish activity. Several of the 3′ : 4′ : 5′ : 6′-tetrahydrodibenzopyrans prepared in the course of model experiments (Part IV; *loc. cit.*) were tested pharmacologically on rabbits and found uniformly inactive by intravenous injection in acetone solution at a dose of 5 mg./kg. of body weight, a dose which is much in excess of the active dose of an ordinary distilled Indian hemp resin. The substances thus examined were 4″-hydroxy-2 : 2-di-

methyl-3′ : 4′ : 5′ : 6′-tetrahydrodibenzopyran, 4″-hydroxy-2 : 2 : 5′-trimethyl-3′ : 4′ : 5′ : 6′-tetrahydrodibenzopyran, the corresponding acetoxy-compounds, and (I; $R_1 = R_2 = Me$).

In preliminary extension of this work we have now synthesised and tested pharmacologically the following compounds: 6″-*hydroxy*-2 : 2-*dimethyl*-4″-n-*amyl*-3′ : 4′ : 5′ : 6′-*tetrahydrodibenzopyran* (*tetrahydronorcannabinol*) (I; $R_1 = H$, $R_2 = C_5H_{11}$), 5″-*hydroxy*-2 : 2 : 5′-*trimethyl*-4″-n-*amyl*-3′ : 4′ : 5′ : 6′-*tetrahydrodibenzopyran* (II), 5-*hydroxy*-2 : 2 : 4-*trimethyl*-7-n-*amyl*-Δ^3-*chromen* (III; $R = C_5H_{11}$), and 5-*hydroxy*-2 : 2-*dimethyl*-7-n-*amyl*-3 : 4-cyclo*penteno*-Δ^3-*chromen* (IV; $R = C_5H_{11}$). Each of these compounds was prepared by the action of excess of methylmagnesium iodide on the corresponding coumarin synthesised by the v. Pechmann method. The biological test results are in the table. 5-*Hydroxy*-2 : 2 : 4 : 7-*tetramethyl*-Δ^3-*chromen* (III; R = Me) and 5-*hydroxy*-2 : 2 : 7-*trimethyl*-3 : 4-cyclo*penteno*-Δ^3-*chromen* (IV; R = Me) were also synthesised in preliminary experiments; (III; R = Me) was not tested pharmacologically.

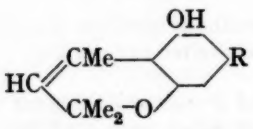
(I.)

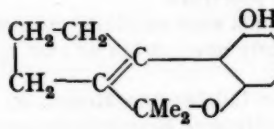




(II.)

(III.)





(IV.)

Substance.	Dose (mg./kg.).	Activity.
Tetrahydrocannabinol ..... (I; $R_1 = Me$, $R_2 = C_5H_{11}$)	1	+
" Tetrahydrocannabinol —165° "	0·3	+
,, ,,	0·1	—
Hexahydrocannabinol	5	+
,, ,, ...	1	—

Substance.	Dose (mg./kg.).	Activity.
Tetrahydronorcannabinol (I; $R_1 = H$, $R_2 = C_5H_{11}$)	5	+
(II)	20	—
(I; $R_1 = R_2 = Me$)	20	—
(III; $R = C_5H_{11}$)	15	—
(IV; $R = C_5H_{11}$)	30	—
(IV; R = Me)	20	—

There has been in the past some disagreement as to the comparability of the various biological tests for *Cannabis* preparations and it was therefore desirable to compare the results of Adams, Loewe, Pease, Cain, Wearn, Baker, and Wolff (*loc. cit.*) on the dog with those obtained by us on the rabbit. The American workers assessed the activity of various materials by comparison with a fraction of distilled " red oil " from American hemp to which was ascribed unit potency. Since our results could not be expressed in the same terms, we prepared " tetrahydrocannabinol, $[\alpha]_D^{22\cdot5°} = -165°$," by cyclisation of cannabidiol as described by Adams, Pease, Cain, and Clark (*J. Amer. Chem. Soc.*, 1940, **62**, 2402) and tested it on rabbits. The results of our tests are, like those in the dog test, only very roughly quantitative and a more accurate assay method is desirable. Nevertheless it can be seen from the table that the cyclised cannabidiol has an activity markedly greater than that of the synthetic tetrahydrocannabinol (I; $R_1 = Me$, $R_2 = C_5H_{11}$). The ratio of the activities of these two compounds in the dog test ($2\cdot15 \pm 0\cdot66/0\cdot20 \pm 0\cdot07$) (Adams, Loewe, Pease, Cain, Wearn, Baker, and Wolff, *loc. cit.*) is higher than in the rabbit test, where it is of the order 5/1. Bearing in mind the very pronounced variation in the response of experimental animals to *Cannabis*, it may be said that the results are qualitatively similar and it would appear likely that the dog and rabbit tests will give comparable results in assessing the hashish activity of synthetic compounds. The few observations which we have made in the dog confirm this impression. Indeed we have so far no reason to doubt that the Gayer response in the rabbit and ataxia in the dog are produced by the same principle, and that this principle can be assayed by either test.

The results recorded in this paper are of too preliminary a nature to warrant any sweeping conclusions as to the structural features necessary for hashish activity, but certain points emerge from them. The activity shown by tetrahydronorcannabinol (I; $R_1 = H$, $R_2 = C_5H_{11}$) and by hexahydrocannabinol, prepared by catalytic hydrogenation of

synthetic tetrahydrocannabinol (I; R = Me, $R_2 = C_5H_{11}$), although less than that shown by (I; R_1 = Me, $R_2 = C_5H_{11}$), indicates that the presence of an alkyl group or a double bond in ring *A* of partly reduced dibenzopyran derivatives is not of primary importance. The orientation of the hydroxyl group (cf. II) and the nature of the side chain in ring *B* (cf. I; $R_1 = R_2$ = Me) seem to be very important. A reduction in the size of ring *A* as in (IV; R = C_5H_{11}) or its complete removal as in (III; R = C_5H_{11}) seems to destroy or at any rate greatly reduce activity. A curious observation made with (IV; R = C_5H_{11}) was that in isolated cases it seemed to show a considerable degree of toxicity. It may be recalled that attention was drawn in Part I (Work, Bergel, and Todd, *Biochem. J.*, 1939, **33**, 123) to the toxic effect of cannabinol in rabbits. In further tests we have been unable to confirm the high degree of toxicity there recorded. We are at a loss to account for this fact, unless it is to be attributed to an unusual degree of sensitivity shown by the strain of animals used in the original experiments.

In the course of experiments carried out in the hope of isomerising synthetic tetrahydrocannabinol (I; R_1 = Me, $R_2 = C_5H_{11}$) by double-bond migration it was observed that irradiation of a sample in ethereal solution with ultra-violet light during 48 hours caused a considerable diminution in hashish activity, although there was little change in absorption spectrum. The nature of the product remains to be determined, but the result may be significant in view of the frequently reported deterioration, also noted by us, of *Cannabis* preparations on keeping.

Experimental.

6-Hydroxy-5'-methyl-7-n-amyl-3 : 4-cyclohexenocoumarin.—*n*-Amylquinol (1·57 g.), prepared by demethylation of its dimethyl ether (Ghosh, Pascall, and Todd, J., 1940, 1118), was suspended in ethyl 1-methyl*cyclo*hexan-3-one-4-carboxylate (1·7 g.), and concentrated sulphuric acid (3 c.c.) gradually added. After 24 hours the solution was poured on ice, and the precipitate collected. Recrystallised from alcohol, the *product* formed pale yellow plates, m. p. 188° (Found : C, 76·4; H, 8·0. $C_{19}H_{24}O_3$ requires C, 76·0; H, 8·0%). On heating with acetic anhydride in pyridine solution the *acetate* was obtained; it crystallised from alcohol in colourless needles, m. p. 119—120° (Found : C, 73·5; H, 7·7. $C_{21}H_{26}O_4$ requires C, 73·7; H, 7·6%).

5''-Hydroxy-2 : 2 : 5'-trimethyl-4''-n-amyl-3' : 4' : 5' : 6'-tetrahydrodibenzopyran (II), prepared from the above acetoxy-coumarin (0·25 g.) by treatment with methylmagnesium iodide (from 0·25 g. of magnesium) in anisole solution, was obtained as a pale yellow resin distilling at 150—160° (bath temp.)/10^{-3} mm. (Found : C, 79·7; H, 9·4. $C_{21}H_{30}O_2$ requires C, 80·2; H, 9·5%). *Light absorption in alcohol :* Maxima at 3280 A. (ε, 5,680) and 2670 A. (ε, 6,190). The *acetate*, prepared in the usual manner, was a pale yellow resin distilling at 150° (bath temp.)/10^{-3} mm. (Found : C, 77·3; H, 8·7. $C_{23}H_{32}O_3$ requires C, 77·5; H, 9·0%).

5-Hydroxy-7-n-amyl-3 : 4-cyclohexenocoumarin.—Condensation of olivetol monohydrate with ethyl *cyclo*hexanone-2-carboxylate in presence of concentrated sulphuric acid gave a *product* crystallising from alcohol in colourless needles, m. p. 180° (Found : C, 75·4; H, 7·9. $C_{18}H_{22}O_3$ requires C, 75·5; H, 7·7%). The *acetate* crystallised from alcohol in colourless plates, m. p. 80° (Found : C, 73·2; H, 7·6. $C_{20}H_{24}O_4$ requires C, 73·1; H, 7·3%).

6''-Hydroxy-2 : 2-dimethyl-4''-n-amyl-3' : 4' : 5' : 6'-tetrahydrodibenzopyran (*Tetrahydronorcannabinol*) (I; R_1 = H, $R_2 = C_5H_{11}$).—The above acetoxycoumarin was treated with excess of methylmagnesium iodide in anisole solution. The *product*, a pale yellow resin, distilled fairly steadily at 158—165° (bath temp.)/10^{-3} mm. (Found : C, 79·1; H, 9·4. $C_{20}H_{28}O_2$ requires C, 80·0; H, 9·4%). *Light absorption in alcohol :* Max. 2740 A. (ε, 10,100).

5-Hydroxy-2 : 2 : 4 : 7-tetramethyl-Δ^3-chromen (III; R = Me).—5-Acetoxy-4 : 7-dimethylcoumarin (v. Pechmann, *Ber.*, 1884, **17**, 2188) was treated with excess of methylmagnesium iodide. On being worked up in the usual way, the *chromen* was obtained as a yellowish resin distilling at 115—120° (bath temp.)/10^{-3} mm., which slowly solidified. Recrystallised from light petroleum, it formed colourless needles, m. p. 97° (Found : C, 75·9; H, 7·8. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·9%). *Light absorption in alcohol :* Max. 2750 A. (ε, 8500).

5-Hydroxy-4-methyl-7-n-amylcoumarin, prepared in the usual manner from ethyl acetoacetate and olivetol monohydrate in presence of concentrated sulphuric acid, formed colourless prisms, m. p. 185°, from alcohol (Found : C, 73·5; H, 7·4. $C_{15}H_{18}O_3$ requires C, 73·2; H, 7·3%). The corresponding *acetate* crystallised from alcohol in needles, m. p. 97° (Found : C, 70·7; H, 6·9. $C_{17}H_{20}O_4$ requires C, 70·8; H, 6·9%).

5-Hydroxy-2 : 2 : 4-trimethyl-7-n-amyl-Δ^3-chromen (III; R = C_5H_{11}).—Prepared by the

action of excess of methylmagnesium iodide on the above acetate in anisole solution, the *product* was a yellowish resin, b. p. 140—150° (bath temp.)/10^{-1} mm. (Found: C, 78·7; H, 9·6. $C_{17}H_{24}O_2$ requires C, 78·5; H, 9·4%).

5-*Hydroxy*-7-*methyl*-3 : 4-cyclo*pentenocoumarin*, prepared as above from ethyl *cyclo*pentanone-2-carboxylate (15·6 g.) and orcinol monohydrate (14·2 g.) in presence of concentrated sulphuric acid (2 g.), formed colourless needles, m. p. 254°, from alcohol (Found: C, 72·2; H, 5·4. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·6%). The *acetate* crystallised from alcohol in needles, m. p. 131° (Found: C, 69·6; H, 5·4. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·4%).

5-*Hydroxy*-2 : 2 : 7-*trimethyl*-3 : 4-cyclo*penteno*-Δ^3-*chromen* (IV; R = Me).—Treatment of the above acetate with excess of methylmagnesium iodide in the normal manner gave a pale yellow resin distilling at 140—150° (bath temp.)/10^{-1} mm. (Found: C, 77·9; H, 8·1. $C_{15}H_{18}O_2$ requires C, 78·3; H, 7·8%). *Light absorption in alcohol:* Max. 2760 A. (ε, 6440).

5-*Hydroxy*-7-n-*amyl*-3 : 4-cyclo*pentenocoumarin*, prepared as above from ethyl *cyclo*pentanone-2-carboxylate and olivetol monohydrate in presence of concentrated sulphuric acid, formed colourless prisms, m. p. 176°, from alcohol (Found: C, 74·8; H, 7·5. $C_{17}H_{20}O_3$ requires C, 74·9; H, 7·4%). The *acetate* crystallised from alcohol in needles, m. p. 65—66° (Found: C, 72·5; H, 6·9. $C_{19}H_{22}O_4$ requires C, 72·6; H, 7·0%).

5-*Hydroxy*-2 : 2-*dimethyl*-7-n-*amyl*-3 : 4-cyclo*penteno*-Δ^3-*chromen* (IV; R = C_5H_{11}).—Prepared by the action of excess of methylmagnesium iodide on the above acetate, the *substance* distilled at 135—140° (bath temp.)/10^{-3} mm. as a pale yellow resin which crystallised on standing. Recrystallised from light petroleum, it formed colourless needles, m. p. 78° (Found: C, 79·8; H, 9·1. $C_{19}H_{26}O_2$ requires C, 79·7; H, 9·1%). *Light absorption in alcohol:* Max. 2790 A. (ε, 11,100).

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UNIVERSITY OF MANCHESTER. [*Received, March 17th*, 1941.]

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37. *Lanosterol. Part II. The Oxidation of Lanosterol with Chromic Acid.*

By LIONEL J. BELLAMY and CHARLES DORÉE.

To throw light on the chemical nature of lanosterol, its reactions with chromic acid, selenium dioxide, and perbenzoic acid have been investigated. The results obtained with chromic acid are described in the present communication.

That bond movement takes place during the formation of the ketone lanostenone is shown (*a*) by its reduction to an isomer of lanosterol, lanosterol-E, and (*b*) by the isolation of a second ketone, *lanostenone-B*, which, since it is reducible smoothly to lanosterol, probably has the same bond system. The acid $C_{25}H_{46}O_2$ has been re-examined, but its saturated character and empirical formula remain in doubt.

THE unsaponifiable fraction of the fat from the wool of the sheep contains considerable quantities of cholesterol together with a second alcohol of high molecular weight, formerly called *iso*cholesterol (Schulze, *Ber.*, 1872, **5**, 1775). The assignment of this substance to the sterol group was based on its origin as a product of animal metabolism. Its isomerism with cholesterol could not be confirmed, as the composition and properties of different preparations did not agree with one another, and it gradually became evident that *iso*cholesterol was not a single compound.

This was confirmed by Windaus and Tschesche (*Z. physiol. Chem.*, 1930, **190**, 59), who showed that crude *iso*cholesterol consists of two unsaturated alcohols, which they named lanosterol, $C_{30}H_{50}O$ (about 90%), and agnosterol, $C_{30}H_{48}O$ (about 10%). Variations in these proportions explained the differences previously recorded in the properties of *iso*cholesterol preparations. Lanosterol was shown to have two double bonds in the molecule, one of which was active and the other inert to catalytic hydrogenation. These results were confirmed by Dorée and Garratt (*J. Soc. Chem. Ind.*, 1933, **52**, 335 T) and by Marker, Wittle, and Nixon (*J. Amer. Chem. Soc.*, 1937, **59**, 1368).

The empirical formula of lanosterol suggested a connection with alcohols of the β-amyrin type rather than with the sterols; the results of dehydrogenation experiments supported this view, and showed that lanosterol did not possess the sterol structure. When heated with palladium charcoal, lanosterol gave a partially dehydrogenated phenanthrene hydrocarbon $C_{18}H_{20}$ (Dorée and Petrow, J., 1936, 1562), and with selenium it yielded 1 : 2 : 8-trimethylphenanthrene (Schulze, *Z. physiol. Chem.*, 1936, **238**, 35). The amyrin series of triterpenes usually yield 1 : 2 : 7-trimethylnaphthalene, 1 : 2 : 5-trimethyl-6-naphthol and 1 : 8-dimethylpicene, but the observation of Drake (*J. Amer. Chem. Soc.*, 1936, **58**, 1681), that friedelin, a triterpene from cork, yields some of these compounds in addition to 1 : 2 : 8-trimethylphenanthrene, indicates that the formation of this hydrocarbon is not incompatible with a triterpenoid structure. A minor point of resemblance between lanosterol and the resinoid alcohols is found in the properties of the monolayer formed by spreading on a water surface. Lanosterol forms an unstable film which rapidly changes to the normal " condensed solid " type (Dorée and Petrow, *loc. cit.*). This unusual phenomenon is shown also by β-amyrin and its derivatives.

Windaus and Tschesche (*loc. cit.*), from the results of perbenzoic acid titrations, concluded that lanosterol possessed two unsaturated centres, one of which was reactive and the other inert to catalytic hydrogenation. Later workers (Dorée and Petrow, J., 1936, 1562; Marker, Wittle, and Nixon, *loc. cit.*) have confirmed this view and the existence in the lanosterol molecule of two unsaturated linkages may be considered as satisfactorily proved.

A doubly unsaturated alcohol, $C_{30}H_{50}O$, must be tetracyclic and, if the relationship of lanosterol to the triterpenes is accepted, a formulation such as (I), based on that of β-amyrin with ring *B* open, may be suggested as a working hypothesis to explain the results obtained in this communication. The formula resembles that of basseol, $C_{30}H_{50}O$, which has been shown by Heilbron, Spring, and others (*Nature*, 1938, **142**, 434; *Chem. and Ind.*, 1939, **58**, 58) and by Ruzicka (*Helv. Chim. Acta*, 1937, **20**, 1553) to have a tetracyclic structure.

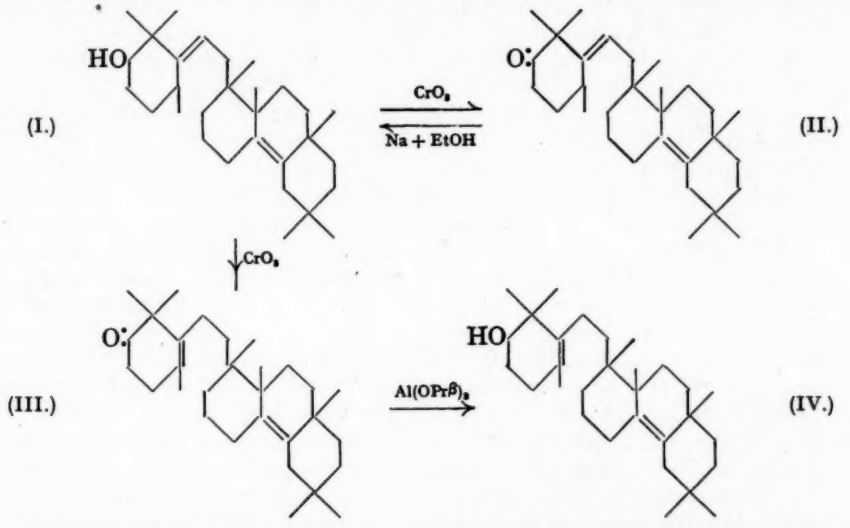
The reactive double link in the tentative lanosterol structure (I) is assigned a position near the hydroxyl group, but not in the same ring. This placing is supported : (*a*) By the observation that the ketones formed from lanosterol are not αβ-unsaturated and therefore the double link cannot be very near to the oxygen atom, even allowing for migration such as occurs during the oxidation of the unsaturated sterol alcohols. (*b*) By the production of the " saturated monobasic non-ketonic acid " $C_{25}H_{46}O_2$ (see p. 174) which results from the oxidation of lanosterol with excess of chromic acid (Marker, Wittle, and Nixon, *loc. cit.*). Its formation, presumably by rupture of the molecule at the position of the active double link, indicates the breakdown of the ring containing the hydroxyl group with the loss of five or perhaps more carbon atoms, and this would be possible on a triterpenoid skeleton if there is adjacent to ring *A* an open ring in which the double link is situated. (*c*) By the analogy of the unimolecular film areas of oxidolanosterol, oxidolanosteryl acetate, and lanostenetriol (Dorée and Petrow, *loc. cit.*), which are of the same order as those of the corresponding derivatives of cholesterol, indicating probably a similar relationship between the position of the hydroxyl group and the double link in both substances.

Agnosterol has been shown by Marker and Wittle (*J. Amer. Chem. Soc.*, 1937, **59**, 2289) to have the same carbon skeleton as lanosterol. It has three unsaturated centres in the molecule, one active and two inert to catalytic hydrogenation. The ultra-violet absorption spectrum indicates that two of these linkings are conjugated (Windaus and Tschesche, *loc. cit.*).

Lanosterol is very sensitive to the action of chromic oxide in acid solution. Windaus and Tschesche (*loc. cit.*) were unable to isolate any crystalline products from normal chromic acid oxidation, but Dorée and Garratt (*loc. cit.*), using specially restrained conditions, isolated in small yield (3%) a ketone, lanostenone, m. p. 115°, together with traces of a second ketone, m. p. 89°, and a non-crystalline monobasic ketonic acid.

Lanostenone on reduction with sodium and ethyl alcohol was said to give an alcohol, lanosterol-A, which was not identical with lanosterol. It was deduced that the bond system of lanostenone differs from that in lanosterol, migration having taken place during oxidation (Dorée and Garratt, *loc. cit.*).

It is now found that by working at room temperature with chromic acid, lanostenone (III) is obtained as a main product (up to 40%). On reduction with aluminium *iso-*



propoxide, a reagent with which bond movement is unlikely, lanostenone gives a new isomer of lanosterol (IV), here designated lanosterol-E.* With sodium and ethyl or propyl alcohol, reduction of lanostenone proceeds further to give α-dihydrolanosterol, the active double bond becoming saturated. This observation proves that the inert double link in lanostenone is in the same position as it is in lanosterol, since an identical product is obtained by the hydrogenation of either substance.

Marker (*loc. cit.*) has also demonstrated the immobility of the inert double bond during oxidation by converting α-dihydrolanosterol into the corresponding ketone and showing that on reduction the original alcohol is obtained. It is therefore the active double bond of lanosterol that migrates, and the fact that it is not adjacent to the hydroxyl group is supported by our observation that lanosterol is unaffected by aluminium *tert.*-butoxide in acetone solution (Oppenauer). The negative result indicates that at least an αβ-position to the hydroxyl group is unlikely. The formation of the acid $C_{25}H_{46}O_2$ by severe oxidation of lanosterol or α-dihydrolanosterol with chromic acid (Marker, Wittle, and Nixon, *loc. cit.*) is also of importance in this connection. The acid is described as monobasic, saturated and non-ketonic. The difficulty of accounting for the formation of an acid with such properties and a formula containing 25 carbon atoms, led us to re-examine the composition and reactions of this substance, but we can only confirm the original statements. The acid proved indifferent to bromine at 0°, to hydrogen (palladium charcoal), and to perbenzoic acid. No carbonyl reactions were given, and the ultra-violet absorption spectrum (Figure) showed general absorption, whereas had an αβ-unsaturated ketonic system been present (which in some triterpenes gives negative reactions), selective absorption would have been expected. The substance requires further critical examination, but its existence indicates a centre in the lanosterol molecule which is open to oxidative attack.

From the mother-liquors of the preparation of lanostenone a second isomeric ketone, m. p. 78°, has been obtained, which is provisionally designated *lanostenone-B*. This ketone on reduction gives lanosterol (I), from which it would appear that lanostenone-B (II) is the ketone corresponding in structure to lanosterol, the mild conditions of oxidation employed allowing a fraction of the alcohol to be converted without bond movement.

The oxidation of lanosteryl acetate with chromic acid was undertaken by Dorée and

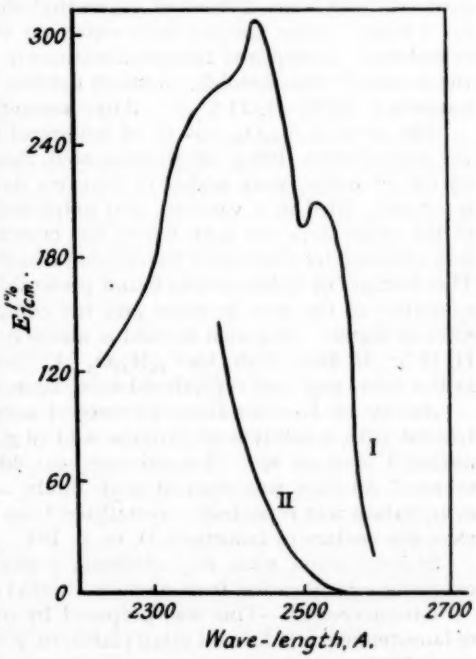
* A series of these isomers has been described. Lanosterol-A is no doubt a mixture of lanosterol-E with α-dihydrolanosterol. Isomers B and C are doubtful. For lanosterol-D, see next page.

Petrow (J., 1936, 1562) in the expectation of converting a methylene group adjacent to an unsaturated linking into a carbonyl group, as examples of this reaction in the triterpene series are well known (Spring and Vickerstaff, J., 1934, 1859; 1937, 249). They obtained unexpectedly the acetate of an alcohol, lanosterol-D, which was stated to be isomeric with lanosterol and to give lanostenone on further oxidation. A repetition of the work shows that lanosteryl-D acetate, m. p. 164°, is certainly formed and that, in the absence of chromic acid, neither glacial acetic acid nor chromic acetate has any effect on lanosteryl acetate.

Professor Marker (private communication) informs us that he has confirmed this result, and has prepared lanosteryl-D acetate, m. p. 164°, but that lanosterol-D itself after extensive purification shrinks at 139—141°, and melts between 155° and 160°, indicating that the limit of purification is not yet reached. Lanosterol-D obtained by us had m. p. 145° and on oxidation with chromic acid gave a ketone, m. p. 105° (tetrahydrocarbazole derivative, m. p. 128°), values which are very different from those given by lanostenone (115° and 202° respectively).

Lanosteryl-D acetate on hydrogenation absorbs one molecular proportion of hydrogen per molecule, giving a dihydrolanosteryl-D acetate, m. p. 218°, differing sharply from α-dihydrolanosteryl acetate (m. p. 119°). The ultra-violet absorption curve given by the acetate of lanosterol-D (Figure) shows strong absorption in the region of 2400—2500 A., indicating that two conjugate double bonds are present.

The action of chromic acid on lanosteryl acetate may possibly bring about the formation of a second inert double bond, in which case lanosterol-D with three double linkings would be an isomer, not of lanosterol, but of agnosterol.



Absorption spectra of (I) *the acetate of lanosterol-D and* (II) *the acid* $C_{33}H_{46}O_2$ (*lanosterol and β-lanostenone similar*).

Experimental.

Analyses by Dr. Weiler, Oxford. Melting points are uncorrected.

Lanostenone: Improved Method of Preparation.—18·5 G. of chromic acid in 190 ml. of water were mixed with 300 ml. of glacial acetic acid, 21 g. of lanosterol in 300 ml. of benzene added, and the whole shaken for 6 hours. After dilution with water the benzene layer was removed, extracted with potassium hydroxide and with water, and dried (sodium sulphate). The benzene solution gave a crystalline mass, which was repeatedly fractionated from acetone–methyl alcohol. Yield, up to 40% of lanostenone.

Lanostenone-B.—The residues from the mother-liquors of the first five crystallisations of the above crude product were fractionated from ethyl alcohol, giving *lanostenone-B* in long needles, m. p. 78°, easily soluble in acetone, benzene and ethyl acetate, less soluble in methyl alcohol (Found: C, 84·3; H, 11·2. $C_{30}H_{48}O$ requires C, 84·8, H, 11·4%). The 2 : 4-dinitrophenylhydrazone formed yellow plates, m. p. 191°. The tetrahydrocarbazole derivative was prepared by warming 0·08 g. of the ketone in 25 ml. of glacial acetic acid with 0·16 g. of phenylhydrazine in 10 ml. of the same solvent for 1 hour on the water-bath. On cooling, colourless crystals separated; these were recrystallised from glacial acetic acid and then had m. p. 178°.

Reduction of Lanostenone-B to Lanosterol.—0·35 G. of lanostenone-B was dissolved in 30 ml. of boiling ethyl alcohol, 1 g. of sodium added as quickly as possible, the solution diluted with 15 ml. of alcohol, and 0·5 g. more of sodium added. The solution was refluxed for 2 hours, poured into water, and extracted with ether. The extract was dried (sodium sulphate), the ether removed, and the product recrystallised from acetone–methyl alcohol (2 : 1), giving lanosterol, m. p. 140—141°, showing no depression on admixture with an authentic specimen.

The acetate, m. p., 114°, and the benzoate, m. p. 187°, of this product were prepared and confirmed its identity with lanosterol.

α-Dihydrolanosteryl Acetate from Lanostenone.—2 G. of lanostenone in 75 ml. of boiling ethyl alcohol were treated rapidly with 3 g. of sodium; 25 ml. of alcohol, and a further 1 g. of sodium were then added. After boiling for 2 hours, the solution was poured into water and extracted with ether. The extract, after drying and removal of the ether, gave a product, which was acetylated by heating with acetic anhydride on the water-bath. The acetate after five crystallisations from ethyl acetate had m. p. 118°, not depressed by authentic α-dihydrolanosteryl acetate kindly supplied by Professor Marker. After saponification α-dihydrolanosterol, m. p. 148°, was obtained.

Lanosterol-E.—4·5 G. of lanostenone were dissolved in 70 ml. of dry *iso*propyl alcohol, and 6 g. of aluminium *iso*propoxide added. The mixture was distilled at the rate of one drop per minute, the distillate giving a positive acetone reaction with sodium nitroprusside in acetic acid. After 8 hours, 200 ml. of 5% methyl-alcoholic potash were added, and the mixture warmed for 1 hour. After pouring into water, an ethereal extract gave a crude product, which was acetylated. It required 20 crystallisations from ethyl acetate and from glacial acetic acid to yield the *acetate* of lanosterol-E, in small needles, m. p. 164° (Found: C, 82·0; H, 11·6. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%). After saponification lanosterol-E was obtained, m. p. 143°.

The Acid $C_{25}H_{46}O_2$.—50 G. of lanosterol in 1 l. of glacial acetic acid were heated to 90° on the water-bath; 100 g. of chromic acid, dissolved in 500 ml. of glacial acetic acid containing 25 ml. of water, were added in portions during 3 hours. On cooling, the solid product was separated, dried in a vacuum, and extracted with ether (Soxhlet). The extract after removal of the ether gave the acid, which was crystallised from methyl ethyl ketone. A further yield was obtained by dilution of the original reaction liquid to turbidity and repetition of the process. This method of isolation was found preferable to that of Marker (*loc. cit.*) owing to the sparing solubility of the acid in ether and the comparative insolubility of the sodium and potassium salts in water. The acid formed a microcrystalline powder, m. p. 81—82° (Found: C, 79·0; H, 12·6; *M*, 388. Calc. for $C_{25}H_{46}O_2$: C, 79·2; H, 12·8%; *M*, 379). The ethyl ester, prepared in the usual way and crystallised from aqueous acetone, had m. p. 64°.

Acetate of Lanosterol-D.—Lanosteryl acetate (10 g.) in glacial acetic acid (150 ml.) was treated with a solution of chromic acid (9 g.) in water (5 ml.), which was added with stirring during 1 hour at 90°. The mixture was diluted with water and extracted with ether. The ethereal solution was washed with dilute acid and dilute alkali. The residue obtained on evaporation was repeatedly crystallised from acetone, ethyl acetate, and glacial acetic acid and gave the acetate of lanosterol-D, m. p. 164°, $[\alpha]_D^{20°}$ (chloroform) + 44°.

Saponification with 5% alcoholic potassium hydroxide gave lanosterol-D, which, after exhaustive purification from acetone–methyl alcohol, had m. p. 145°.

Lanostenone-D.—This was prepared by oxidation with chromic acid as in the preparation of lanostenone. It formed small plates, m. p. 105° (tetrahydrocarbazole derivative, white plates, m. p. 128°).

Acetate of Dihydrolanosterol-D.—The acetate of lanosterol-D (0·2 g.) in glacial acetic acid (25 ml.) was shaken with hydrogen at 20° for 6 hours, palladium charcoal (0·05 g.) being used as catalyst. Hydrogen equivalent to one double bond was absorbed. The product crystallised from glacial acetic acid in small needles, m. p. 218°, slightly soluble in methyl alcohol and glacial acetic acid.

Non-action of the Oppenauer Reagent on Lanosterol.—10 G. of lanosterol in 100 ml. of hot acetone were mixed with a solution of 12 g. of crystalline aluminium *tert.*-butoxide in 300 ml. of acetone and refluxed for 10 hours. The product, isolated in the usual way, consisted of unchanged lanosterol.

CHELSEA POLYTECHNIC, LONDON, S.W. 3. [*Received, August 13th*, 1940.]

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38. *Lanosterol. Part III. The Action of Selenium Dioxide and of Perbenzoic Acid on Lanosterol.*

By LIONEL J. BELLAMY and CHARLES DORÉE.

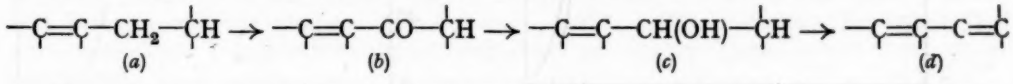
The presence of a methylene group adjacent to the active double bond in lanosteryl acetate is shown by the action of selenium dioxide, which gives a *diol* capable of forming a *diacetate*. With α-dihydrolanosteryl acetate, selenium dioxide gives a *monoacetate*,

$C_{32}H_{52}O_2$, indicating that dehydration has taken place with the introduction of a new double bond. This was confirmed by hydrogenation of the compound, one molecular proportion of hydrogen being absorbed and α-dihydrolanosterol obtained. The properties of the acetate $C_{32}H_{52}O_2$ closely resemble those of α-dihydroagnosterol acetate and the two substances may be identical.

The oxide produced by the action of perbenzoic acid on lanosteryl acetate (J., 1936, 1562) can be hydrolysed to give a *triol*, one of the hydroxyl groups of which is tertiary, indicating that the active double link in lanosterol is of the type >C=CH—. Lanostenone also formed an *oxide*, and on treatment with alcoholic hydrochloric acid simultaneous hydrolysis and dehydration took place, a *dehydro*-derivative, $C_{30}H_{44}O$, being obtained in which three double bonds were present. One of these, only, could be hydrogenated and, as the absorption spectrum of the dihydro-derivative shows that the two inactive double bonds are conjugated, this compound resembles α-dihydroagnosterol. The results throw light on the bond systems of lanosterol and agnosterol.

Selenium Dioxide.—The action of selenium dioxide on the unsaturated members of the sterol group first studied by Rosenheim and Callow (J., 1933, 387) is normally one of two types. In the first, oxidation of a methylene group adjacent to the unsaturated linkage takes place, a hydroxyl group being introduced. Cholesterol, for example, with selenium dioxide gives Δ^5-cholestene-3:4 diol (Rosenheim and Starling, J., 1937, 377), which undergoes in the course of the reaction an allylic rearrangement to Δ^4-cholestene-3 : 6-diol (Petrow, Rosenheim, and Starling, J., 1938, 679). The second type leads to the formation of a new unsaturated centre in the molecule, probably owing to dehydration at the position of a hydroxyl group primarily introduced. The bond originally present sometimes migrates, but in the resulting diene the bonds are always conjugated.

Lanosterol, $C_{30}H_{50}O$, with one active and one inert double bond occurs in association with the structurally similar alcohol agnosterol, $C_{30}H_{48}O$, which has one active and two inert double bonds. Reaction of lanosterol with selenium dioxide might be expected to lead to the formation of agnosterol or its isomers, either by the introduction of a new double linking, or by the production of a hydroxy-compound which could subsequently be dehydrated to produce one. The latter probability is supported by the work of Marker, Wittle, and Nixon (*J. Amer. Chem. Soc.*, 1937, **59**, 1368), who by the action of chromic acid on a methylene group adjacent to the inert double bond in α-dihydrolanosteryl acetate obtained a keto-acetate which on reduction and dehydration gave α-dihydroagnosteryl acetate identical with that prepared from natural agnosterol by catalytic hydrogenation (see scheme, p. 179). There is therefore a methylene group adjacent to the inert double bond of α-dihydrolanosterol, and the reactions described may be represented thus :



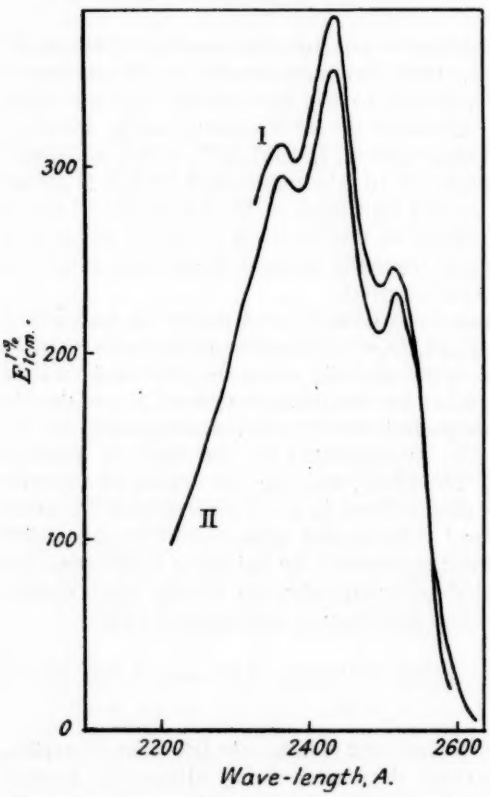
A similar conversion has been carried out with β-amyrenyl benzoate (Beynon, Sharples, and Spring, J., 1938, 1233), a dehydro-β-amyrenyl derivative being ultimately formed which is resistant to catalytic hydrogenation.

Selenium dioxide reacted vigorously with lanosteryl acetate in alcoholic solution. The products gave in small yield the *monoacetate* of a diol, $C_{32}H_{52}O_3$, which on saponification gave the *diol*, $C_{30}H_{50}O_2$, m. p. 143·5°. The diol on acetylation gave a *diacetate*, which proves that dehydration could not have occurred. If the hydroxyl group had occupied the same position as it does in the hydroxydihydrolanosteryl acetate prepared by Marker (*loc. cit.*), it would have participated in dehydration, so the methylene groups attacked in the two cases are not the same. The methylene group concerned in the formation of the diol $C_{30}H_{50}O_2$ is therefore the one adjacent to the active double bond, whereas that oxidised in producing hydroxydihydrolanosterol is adjacent to the inactive double bond. The possibility that selenium dioxide might have reacted with methylene groups activated by each of the double bonds of lanosterol was indicated by the isolation from the mother-liquors, of a second *diol*, m. p. 152°. The yield, however, was so small that no conclusions could be drawn, and to throw further light on the question the action of selenium dioxide

on α-dihydrolanosteryl acetate, in which the inactive double bond of lanosterol alone remains, was examined.

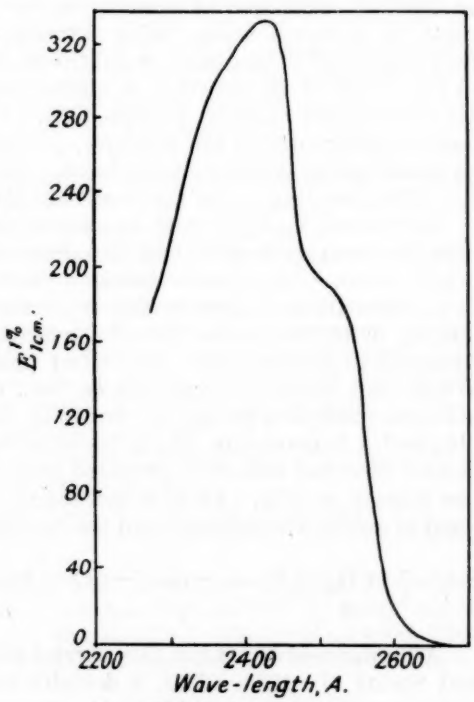
Selenium dioxide did not react with α-dihydrolanosteryl acetate in alcohol or glacial acetic acid at 100°. By using a large excess of the reagent in boiling glacial acetic acid, however, interaction took place and a *monoacetate*, $C_{32}H_{52}O_2$, m. p. 167°, was obtained in the high yield of 40%. Its composition showed that in this case a new double bond had been introduced, which was confirmed by catalytic hydrogenation, hydrogen equivalent to one molecular proportion being absorbed and α-dihydrolanosteryl acetate obtained in quantitative yield. The monoacetate, m. p. 167°, is thus a dehydro-derivative of α-dihydrolanosteryl acetate, and therefore an isomer of lanosteryl acetate. It has accordingly been termed γ-lanosteryl acetate, giving a γ-lanosterol, m. p. 141°.

FIG. 1.



Absorption spectra of (I) *γ-lanosteryl acetate, and* (II) *α-dihydroagnosteryl acetate.*

FIG. 2.



Dehydrolanostenone.

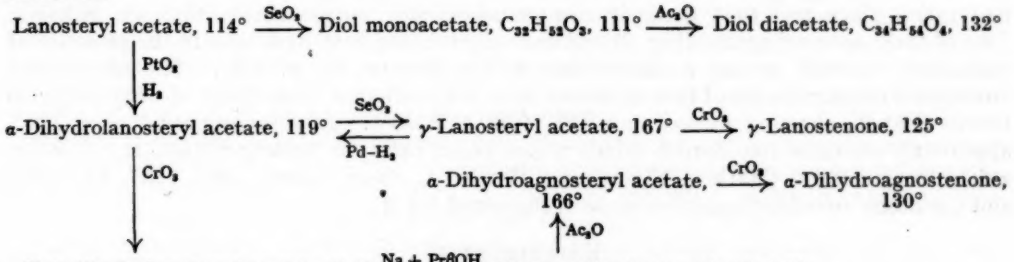
In analogy with similar reactions in the sterol series it was expected that the double bonds in γ-lanosterol would be conjugated. The ultra-violet absorption curve (Fig. 1) confirmed this, a well-defined maximum at 2450 A. being observed. The inert double bond of γ-lanosterol is almost certainly in its original position, although the reduction to α-dihydrolanosterol is not entirely conclusive, as the addition of hydrogen to conjugate systems in the 1 : 4-position sometimes occurs. γ-Lanosterol, if not identical with α-dihydroagnosterol, must be very closely related to it. The action of selenium dioxide on α-dihydrolanosteryl acetate being assumed to follow the normal course, it would be explained by a similar scheme to that used above in the case of the conversion of α-dihydrolanosteryl acetate into α-dihydroagnosteryl acetate by Marker, Nixon, and Wittle (*loc. cit.*), stage (*b*) being omitted, and γ-lanosterol would be identical with α-dihydroagnosterol. It will be

noted (Fig. 1) that the ultra-violet absorption curves of the two substances are practically identical and the following table shows the similarity in the melting points of the two compounds and their derivatives. The acetates of this group have always proved the most suitable material for purification and the melting points of α-lanosteryl and α-dihydroagnosteryl acetates are not only equal, but they give no depression on admixture. The alcohol γ-lanosterol may contain an epimer, which would account for the lower melting point.

	Alcohol.	Acetate.	Ketone.
α-Dihydroagnosterol	150°	166—167°	130°
γ-Lanosterol	141	167	124

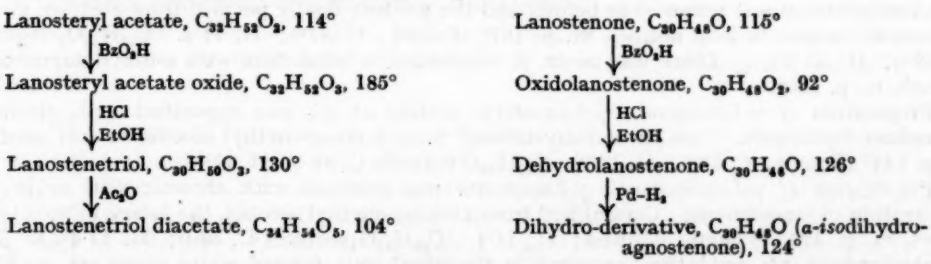
Against this apparent identity must be placed the smooth hydrogenation of γ-lanosterol to α-dihydrolanosterol when a palladium catalyst is used. Agnosterol, when reduced with hydrogen in the presence of platinum, gives only the dihydro-derivative with two conjugate double bonds. Thus one only of the double bonds of γ-lanosterol resists catalytic hydrogenation, whereas, apparently, in the case of α-dihydroagnosterol, both do so.

These reactions connecting lanosterol with agnosterol are summarised in the following scheme, which includes the observations of Marker, Nixon, and Wittle (*loc. cit.*) and ourselves.



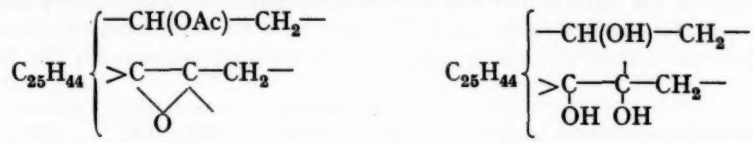
Perbenzoic Acid.—The action of perbenzoic acid has afforded useful evidence regarding the number and nature of the unsaturated linkages present in the sterols and resin alcohols. Cholesterol, for example, gives an oxide which on hydrolysis yields 3 : 5 : 6-trihydroxycholestane. The position of the original double bond is thus made evident. On acetylation a diacetate is obtained, which under the action of suitable dehydrating agents loses the elements of water, giving rise to an unsaturated linking in a new position. Dehydration at one (or both) of the hydroxy-groups of α-glycols such as 3 : 5 : 6-trihydroxycholestane is generally produced by the action of acetic anhydride, but frequently less active reagents will bring about the change. Heilbron (J., 1934, 1577), for example, found that ergostadienetriol I passes into dehydroergosterol on simple crystallisation from glacial acetic acid.

Petrow (J., 1939, 1000) also reports that during the hydrolysis of 5-methylnorcholestane-3 : 6-diol 8 : 9-oxide with alcoholic hydrochloric acid, dehydration of both hydroxyl groups takes place, giving a dehydro-derivative, 5-methyl-$\Delta^{9:11,\ 8:14}$-norcholestadiene-3 : 6-diol. The reactions of lanosterol and lanostenone with perbenzoic acid can be explained on similar lines. They are summarised in the scheme given below.



Lanosteryl acetate, when treated with perbenzoic acid, gave the lanosteryl acetate

oxide described by Dorée and Petrow (J., 1936, 1562). The melting point, however, proved to be 185°, instead of 178° as recorded by them. Treatment with alcoholic hydrochloric acid opened the oxide ring with the production of an α-glycol, thus :—



A *lanostenetriol*, $C_{30}H_{50}O_3$, was obtained, which, on acetylation, gave a *diacetate*. The two hydroxyl groups acetylated must be of the secondary type, one being that originally present in lanosterol, and the second, one of those introduced at the position of the double bond. The other non-reactive hydroxyl introduced must be tertiary, and in consequence the double bond at which the hydroxyls were situated is of the type >C=CH—.

Lanostenone, when treated with perbenzoic acid equivalent to one atom of oxygen per molecule, reacted very slowly to give an *oxide*, $C_{30}H_{48}O_2$, m. p. 92°. Hydrolysis with alcoholic hydrochloric acid was expected to yield a keto-diol, but instead a *dehydro*-derivative of lanostenone, $C_{30}H_{46}O$, was obtained, a result indicating that hydrolysis and dehydration had taken place and that the new compound should contain three ethylenic linkages. Two of these are conjugated (Fig. 2) and one only reacted with hydrogen in the presence of palladium charcoal, giving a dihydrodehydrolanostenone, m. p. 124°. The ultra-violet absorption measurements of this substance were very different from those of dehydrolanostenone (Fig. 2), showing a maximum $E^{1\%}_{1\,cm.}$ of 60 at 2400 A. As this compound, m. p. 124°, apparently contains two double bonds which resist catalytic hydrogenation, it resembles α-dihydroagnosterol (Marker, Nixon, and Wittle, *J. Amer. Chem., Soc.*, 1937, **59**, 2289) and the name α-*iso*dihydroagnostenone is suggested for it.

Experimental.

Action of Selenium Dioxide on Lanosteryl Acetate.—To lanosteryl acetate (4 g.), dissolved in boiling ethyl alcohol (100 ml.), was added selenium dioxide (1·1 g.) in a little water. After being refluxed for 1 hour and filtered hot, the liquid was poured into water and extracted with ether. Residual selenium was removed by treatment with potassium cyanide solution, and the ethereal solution washed with water and dried. After removal of the ether, the product was repeatedly crystallised from methyl alcohol, and gave a small quantity of the *diol monoacetate*, in needles, m. p. 110° (Found : C, 79·5; H, 10·7. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). The acetate was saponified, giving the *diol*, which crystallised from acetone–methyl alcohol in felted needles, m. p. 143—144° (Found : C, 81·8; H, 11·9. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·3%). The diol on acetylation gave the *diol diacetate*, which formed large plates from acetone–methyl alcohol, m. p. 132° (Found : C, 76·6; H, 10·0. $C_{34}H_{54}O_4$ requires C, 77·5; H, 10·2%).

Preparation of the Diol, $C_{30}H_{50}O_2$, m. p. 152°.—The mother-liquors from the first five crystallisations of the initial product were bulked and saponified. Crystallisation from ethyl acetate gave a very small quantity of a *diol*, m. p. 152° (Found : C, 81·6; H, 11·7. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·3%).

Action of Selenium Dioxide on α-Dihydrolanosteryl Acetate.—α-Dihydrolanosteryl acetate (2 g.) in glacial acetic acid (200 ml.) was treated with selenium dioxide (2 g.) in a little water. The mixture was refluxed for 3 hours, sodium acetate then added, and the solution filtered hot. Residual selenium was removed as before, and the product finally purified from acetone, giving *γ-lanosteryl acetate* in long needles, m. p. 167° (Found : C, 81·9; H, 11·2. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%). There was no m. p. depression in admixture with α-dihydroagnosteryl acetate, m. p. 166°.

Preparation of γ-Lanosterol.—γ-Lanosteryl acetate (1 g.) was saponified with alcoholic potassium hydroxide. The *product* crystallised from acetone–methyl alcohol in soft needles, m. p. 141° (Found : C, 83·9; H, 12·0. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%).

Preparation of γ-Lanostenone.—γ-Lanosterol was oxidised with chromic acid as in the preparation of lanostenone. Crystallised from acetone–methyl alcohol, the *ketone* formed large plates, m. p. 124° (Found : C, 84·4; H, 11·4. $C_{30}H_{48}O$ requires C, 84·9; H, 11·4%). The tetrahydrocarbazole derivative, prepared in the usual way, formed white plates, m. p. 228°, from benzene–alcohol.

Formation of α-Dihydrolanosteryl Acetate from γ-Lanosteryl Acetate.—A mixture of γ-lanosteryl acetate (0·2 g.) in purified glacial acetic acid (25 ml.) with stabilised palladium charcoal (0·05 g.) was shaken for 6 hours with hydrogen at atmospheric pressure. After filtering, the product was isolated by dilution to turbidity; on cooling, α-dihydrolanosteryl acetate separated in long needles, m. p. 118°. It gave no m. p. depression on admixture with an authentic specimen and after saponification α-dihydrolanosterol, m. p. 148°, was obtained showing similar identity.

Preparation of Lanosteryl Acetate Oxide.—Lanosteryl acetate (5 g.) in chloroform (50 ml.) was treated with a chloroform solution of perbenzoic acid equivalent to 0·2 g. of active oxygen during ½ hour at 0°. After 24 hours at 0° the solvent was removed, and the oxide taken up in ether. Repeated purification from ethyl acetate gave lanosteryl acetate oxide, m. p. 185°.

Lanostenetriol.—Lanosteryl acetate oxide (0·5 g.) in ethyl alcohol (30 ml.) was treated with hydrochloric acid (2 ml.) and water (2 ml.) and refluxed for 3 hours. After dilution to turbidity *lanostenetriol* crystallised on cooling, and was purified from acetone solution. It formed white plates, m. p. 130°, easily soluble in benzene and ether, and slightly soluble in methyl alcohol (Found: C, 78·8; H, 11·3. $C_{30}H_{50}O_3$ requires C, 79·0; H, 10·9%).

Diacetate of Lanostenetriol.—Lanostenetriol (0·2 g.) in acetic anhydride (10 ml.) was heated for 1 hour. The *product*, recrystallised from glacial acetic acid, gave white plates, m. p. 104° (Found: C, 75·5; H, 10·3. $C_{30}H_{54}O_5$ requires C, 75·3; H, 9·9%).

The Action of Perbenzoic Acid on Lanostenone.—Lanostenone (5 g.) was treated with a solution of perbenzoic acid as above. The product was fractionally crystallised from methyl alcohol to remove unchanged lanostenone, which formed the least soluble fraction. The mother-liquors gave *lanostenone oxide*, m. p. 92°, readily soluble in benzene, acetone, and ethyl acetate (Found: C, 81·6; H, 11·5. $C_{30}H_{48}O_2$ requires C, 81·7; H, 10·9%).

Dehydrolanostenone.—Lanostenone oxide (0·2 g.) was hydrolysed with alcoholic hydrochloric acid as described above. The *product*, crystallised from acetone–methyl alcohol, gave white plates, m. p. 126° (Found: C, 84·5; H, 11·2. $C_{30}H_{46}O$ requires C, 85·0; H, 11·0%). The tetrahydrocarbazole derivative had m. p. 228°, and the oxime m. p. 183°.

iso*Dihydroagnostenone.*—Dehydrolanostenone (0·2 g.) in glacial acetic acid (25 ml.) was shaken with hydrogen for 6 hours at 20°, palladium charcoal (0·05 g.) being used as catalyst. Hydrogen equivalent to one double bond was absorbed. The compound crystallised from glacial acetic acid in plates, m. p. 124°, and formed a tetrahydrocarbazole derivative, m. p. 202°, and an oxime, m. p. 164°.

CHELSEA POLYTECHNIC, LONDON, S.W. 3. [*Received, August 12th*, 1940.]

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39. *The Triterpene Group. Part VIII. The Minor Triterpenoid Constituents of* Manila elemi *Resin (continued).*

By ISOBEL M. MORICE and JAMES C. E. SIMPSON.

Previous work (Morice and Simpson, J., 1940, 795) pointed to the existence in *Manila elemi* resin of a precursor of ψ-taraxasterol. The precursor, *ψ-taraxastanediol*, has now been isolated. It is a saturated dihydric alcohol containing a tertiary hydroxyl group, and it is converted by means of hot formic acid into ψ-taraxasteryl formate, the reaction being one of dehydration. The biogenetic relationship thus disclosed is novel to the triterpene series.

Very small quantities of two further new alcohols have been isolated from the resin; these are a *diol*, m. p. 236°, and an *alcohol*, m. p. 254°, containing an uncharacterised oxygen atom, and their probable formulæ are $C_{30}H_{48}O_2$ and $C_{30}H_{54}O_2$ respectively.

IN Part VII (Morice and Simpson, *loc. cit.*) we described the isolation of ψ-taraxasterol from *Manila elemi* resin. On the basis of the evidence then available, it seemed unlikely that this alcohol existed as such in the resin, particularly since the employment of formic acid, which is well known as an isomerising agent in the triterpene series (Beynon, Heilbron, and Spring, J., 1937, 989; Zimmermann, *Helv. Chim. Acta*, 1938, **21**, 853), appeared to be a *sine qua non* for the successful isolation of the compound; we accordingly postulated the existence in *Manila elemi* resin of an isomeric precursor of ψ-taraxasterol. We have now

achieved the isolation of this precursor under conditions which do not involve the use of formic acid, and have demonstrated its facile conversion into ψ-taraxasterol by subsequent treatment of it with this acid.

Contrary to expectation, however, ultimate analysis showed that the new compound has the molecular formula $C_{30}H_{52}O_2$; its conversion into ψ-taraxasterol is therefore not an isomerisation, but a dehydration. We have named the precursor *ψ-taraxastanediol* in order to indicate its relationship to ψ-taraxasterol and also to show that it has the character of a saturated dihydric alcohol. The saturated nature of the substance follows from the facts (*a*) that its acetate does not react with perbenzoic acid, in contrast to the conversion of ψ-taraxasteryl acetate into an *oxide* under similar conditions; and (*b*) that it is inert towards tetranitromethane and is also transparent to ultra-violet light. Both oxygen atoms in the molecule of ψ-taraxastanediol are present as hydroxyl groups (Zerewitinoff), but only one (*i.e.*, that contained in ψ-taraxasterol) is esterifiable under ordinary conditions; the other is therefore presumably tertiary, a supposition which explains both its inertness towards acetic anhydride (in pyridine) and also its ready elimination as water under the influence of hot formic acid.

ψ-Taraxastanediol and ψ-taraxasterol represent a new biogenetic relationship in the triterpene series, which is comparable with the classical α-terpineol–terpinolene relationship in the simple terpenes. The diol is isomeric with zeorin, which has been shown by Asahina and Akagi (*Ber.*, 1938, **71**, 980) to belong to the triterpene group. Like ψ-taraxastanediol, zeorin readily undergoes dehydration (the authors employed boiling acetic anhydride, but did not report on the behaviour of the diol towards formic acid), but the product, anhydrozeorin, is not known to occur in Nature.

It is somewhat remarkable that ψ-taraxastanediol is more strongly adsorbed on alumina (see Experimental) than the unsaturated diols breïn and maniladiol; it would appear that spatial factors may over-ride purely structural considerations in the formation of complexes between molecules of alumina and these substances.

In the course of the search for ψ-taraxastanediol, small amounts of two new, lævorotatory alcohols were isolated. The first of these, which we have provisionally named *diol A*, was obtained from the fractions immediately preceding those containing ψ-taraxastanediol. The presence of two esterifiable hydroxyl groups in diol A was shown by the preparation of the *diacetate*, and analyses of this ester and of the parent diol suggest the formula $C_{30}H_{48}O_2$ for the latter. The second compound, *alcohol B*, formed only a *monoacetate*; it appears from analysis to have the formula $C_{30}H_{54}O_2$, but behaves as an unsaturated compound despite its high hydrogen content. The small quantities of diol A and alcohol B which were available, however, precluded further investigation, and consequently their molecular formulæ cannot be deemed to be established with certainty.

Experimental.

(Melting points are uncorrected. Specific rotations are in chloroform solution. The ligroin used had b. p. 80—100° except where otherwise stated.)

The material employed in this investigation consisted mainly of the non-crystalline residue remaining after fraction X (Morice and Simpson, *loc. cit.*) had been acetylated and the crystalline product removed, together with smaller quantities of similar residues from fractions VI—IX. The solvent-free material (65 g.) was refluxed for 2 hours with alcoholic potassium hydroxide (2%, 975 c.c.), the free alcohols (54 g.) being isolated by precipitation with water and extraction with ether. After careful drying and removal of solvent, the residue was dissolved in benzene–ligroin (2700 c.c., 7 : 3) and filtered through a column (120 × 4 cm.) of alumina (1350 g. of Merck's, " standardisiert nach Brockmann "), which had been prepared from a suspension in benzene–ligroin (7 : 3). The column was then washed with successive portions of solvent mixtures of various compositions, following on general lines the procedure of Reichstein and von Euw (*Helv. Chim. Acta*, 1939, **22**, 1222). Fractions 1—7 (see Table) showed no tendency to crystallise, and were not examined further. Fractions 8—35 were separately acetylated by heating the material (1 part) on the water-bath with pyridine (2 parts) and acetic anhydride (1 part) for 2 hours. The acetates were obtained by precipitation with water, followed by extraction with ether or by filtration. Continued recrystallisation (from aqueous alcohol, alcohol, or benzene–alcohol) of the crude products led to the isolation of the following acetates,

listed in increasing order of adsorbability : β-Amyrin (0·25 g.), ψ-taraxasterol (0·43 g.), a mixture of breïn and maniladiol (6·4 g.), diol A (0·05 g.), ψ-taraxastanediol (1·0 g.), and alcohol B (0·1 g.). The conditions employed enabled a much more complete separation to be achieved than in our earlier work (*loc. cit.*), but formylation was still necessary to effect the resolution of the breïn–maniladiol mixture.

TABLE.

Fraction.	Washing solvent (in c.c.).	Weight (g.) of recovered material.	Description.	Alcohol (isolated as acetate).
1	Original filtrate	0·35	Resinous	—
2	Benzene–ligroin (7 : 3), 1080	0·54	,,	—
3	,, (8 : 2), 1080	0·38	,,	—
4	,, (9 : 1), 1080	0·15	,,	—
5	Benzene, 1080	0·56	,,	—
6	,, , 1080	0·82	,,	—
7	,, , 2160	2·11	,,	—
8	,, ,,	3·30	Crystalline	β-Amyrin
9	,, ,,	2·76	,,	ψ-Taraxasterol
10	,, ,,	2·11	Resinous	,,
11	,, ,,	2·52	Frothy	Breïn–maniladiol
12	,, ,,	2·73	,,	,,
13	,, ,,	2·41	,,	,,
14	,, ,,	2·14	,,	,,
15	,, ,,	1·70	,,	,,
16	,, ,,	1·65	,,	,,
17	,, ,,	1·24	Crystalline	,,
18	,, ,,	1·20	,,	,,
19	,, ,,	0·77	,,	,,
20	Ether–benzene (1 : 5·6), 2870	1·93	Gelatinous	Diol A
21	,, (1 : 4), 2160	2·16	,,	,,
22	,, ,, ,,	1·72	,,	,,
23	,, ,, ,,	1·42	,,	ψ-Taraxastanediol
24	,, ,, ,,	1·05	Crystalline	,,
25	,, (2 : 5), ,,	1·26	,,	,,
26	,, ,, ,,	1·96	,,	,,
27	,, ,, ,,	1·75	,,	,,
28	,, ,, ,,	1·24	Resinous	
29	,, ,, ,,	0·48	,,	—
30	,, (1 : 1), ,,	0·29	,,	—
31	,, ,, ,,	0·15	,,	—
32	Ether ,,	0·23	,,	—
33	,, ,,	0·22	,,	—
34	Ether–acetone (3 : 1), 2160	2·31	,,	Alcohol B
35	,, ,, ,,	2·19	,,	—

Monoacetate of ψ-Taraxastanediol.—This *compound* crystallised from benzene–alcohol in prismatic needles, m. p. 281—284° (with slight discoloration), $[\alpha]_D^{23°}$ −1·5° ($l = 1$, $c = 1·01$) (Found : C, 78·8; H, 11·3. $C_{32}H_{54}O_2$ requires C, 78·9; H, 11·2%). *Active hydrogen determination (Zerewitinoff) :* 4·022 Mg. gave 0·20 c.c. of methane at 21°/778 mm., corresponding to 1·03 active hydrogen atom.

Hydrolysis of this acetate with boiling 2% alcoholic potassium hydroxide gave *ψ-taraxastanediol*, which separated from benzene in small dense prisms, and from alcohol in soft matted needles; m. p. 270—272° (discoloration), $[\alpha]_D^{23°}$ −10·9° ($l = 1$, $c = 1·105$) (Found : C, 81·1; H, 11·9. $C_{30}H_{52}O_2$ requires C, 81·0; H, 11·8%). Owing to its ready dehydration, the alcohol gave a Liebermann–Burchard reaction (pink, changing to purplish-red with a green fluorescence) indistinguishable from that of ψ-taraxasterol. The tetranitromethane reaction in chloroform was negative.

Dehydration of ψ-Taraxastanediol.—(*a*) The monoacetate was refluxed for 2 hours with benzene (20 parts) and formic acid (20 parts). Water was then added, and the benzene layer, after addition of ether, followed by washing with 2% aqueous sodium carbonate and water, was dried and evaporated. The residue crystallised from alcohol in shining plates, m. p. 237—239°, $[\alpha]_D^{23°}$ +52° ($l = 1$, $c = 1·30$); no lowering of melting point was observed when this material was mixed with authentic ψ-taraxasteryl acetate of the same m. p. and $[\alpha]_D$ +53°.

(*b*) ψ-Taraxastanediol was refluxed for 2 hours with benzene (80 parts) and formic acid (80 parts). The resultant ψ-taraxasteryl formate, isolated as described above, separated in needles from benzene–alcohol; it had m. p. 219—220°, $[\alpha]_D^{23°}$ +48° ($l = 1$, $c = 1·89$), and did not depress the m. p. (219—221°) of an authentic specimen ($[\alpha]_D$ + 51°; Morice and Simpson, *loc. cit.*).

(*c*) The extreme ease with which ψ-taraxastanediol undergoes dehydration was illustrated by an attempt to benzoylate the diol. A solution of the compound (1 part) in pyridine (40 parts) and benzoyl chloride (10 parts) was heated at 100° for 2 hours; water was then added, and the product extracted with ether. The extract was washed successively with dilute acetic acid, dilute sodium hydroxide solution, and water. The residue obtained by evaporation of the dried solution had m. p. 259—263°, $[\alpha]_D^{19°}$ +57° ($l = 1$, $c = 1{\cdot}21$), and a mixture of it with authentic ψ-taraxasteryl benzoate (m. p. 280—282°, $[\alpha]_D$ +68°) melted at 266—275°.

Diacetate of Diol A.—Continued recrystallisation of the combined crystalline acetates from fractions 20—22 involved large losses of material without achieving the isolation of any single substance. The various fractions were therefore again combined (2·2 g.) and hydrolysed with boiling alcoholic potassium hydroxide (100 c.c. of 2%). The mixture of alcohols, isolated by means of ether, was dissolved in benzene (160 c.c.), and the solution was drawn through a column (55 × 1·4 cm.) of activated alumina (Merck, 80 g.). By fractional elution with 80 c.c. portions of benzene, benzene–ether, and acetone, the material was divided into 21 sub-fractions. These were acetylated, either separately or in pairs, but no apparent purification was accomplished in the majority of cases. However, sub-fractions 10, 11, and 12 yielded acetates, which were combined after one crystallisation (0·21 g.) and crystallised a further five times from aqueous alcohol and finally from ligroin (b. p. 40—60°). The *diacetate* of diol A was thus obtained as small prisms (50 mg.), m. p. (constant) 211—212°, $[\alpha]_D^{19°}$ + 35° ($l = 1$, $c = 1{\cdot}68$) (Found: C, 78·2; H, 10·35. $C_{34}H_{52}O_4$ requires C, 77·8; H, 10·0%).

Diol A.—The foregoing acetate (40 mg.) was refluxed for 2 hours with alcoholic potassium hydroxide (10 c.c. of 2%). The solution was then concentrated to half volume, diluted with water, and extracted with ether. Evaporation of the washed and dried extract furnished *diol A*, which after two crystallisations from ether–ligroin (b. p. 40—60°) formed clusters of needles, m. p. 234—236°, $[\alpha]_D^{22°}$ −70°±10° ($l = 1$, $c = 0{\cdot}145$) (Found: C, 82·15; H, 11·3. $C_{30}H_{48}O_2$ requires C, 81·75; H, 11·0%). The diol gave a yellow colour with tetranitromethane in chloroform, and the Liebermann–Burchard reagent produced an orange-red coloration, which changed to brownish-pink with a green fluorescence.

Monoacetate of Alcohol B.—Continued recrystallisation from alcohol of the crude acetate from fraction 34 finally yielded the *monoacetate* as rectangular prisms, m. p. 227—229°, $[\alpha]_D^{23°}$ −39° ($l = 1$, $c = 1{\cdot}38$) (Found: C, 78·45; H, 11·4. $C_{32}H_{56}O_3$ requires C, 78·6; H, 11·5%).

Alcohol B.—Hydrolysis of the monoacetate (60 mg.) with 2% alcoholic potash (10 c.c.), followed by precipitation with water and recrystallisation of the product from aqueous methanol, gave *alcohol B*, which separated in needles, m. p. 252—254°, $[\alpha]_D^{19°}$ −17° ($l = 1$, $c = 1{\cdot}10$) (Found: C, 80·1; H, 11·8. $C_{30}H_{54}O_2$ requires C, 80·65; H, 12·2%). Addition of tetranitromethane to a chloroform solution of the alcohol gave a very pale yellow solution, and the Liebermann–Burchard reagent produced a magenta coloration.

ψ-Taraxasteryl Acetate Oxide.—ψ-Taraxasteryl acetate was dissolved in a large excess of an approximately 0·3N-solution of perbenzoic acid in chloroform, and the solution was set aside (with accompanying blank experiment) for 10 days; titration then showed that 0·9 atom of active oxygen had been absorbed. The solution was washed with aqueous sodium carbonate and water, dried, and evaporated, and the residue crystallised from alcohol; *ψ-taraxasteryl acetate oxide* separated in lustrous plates, which melted at 265—267°, and then resolidified and again melted at 300° (Found: C, 79·3; H, 11·0. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%).

We are indebted to Dr. R. A. Morton for the spectrographic examination of ψ-taraxastanediol, and to the Chemical Society for a grant.

DURHAM COLLEGES IN THE UNIVERSITY OF DURHAM. [*Received, February 28th,* 1941.]

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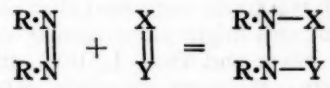
40. cis-*Azo-compounds. Part IV. Some Reactions with Diphenylketen.*

By A. H. COOK and D. G. JONES.

cis- and *trans*-Azo-compounds have been shown to be sharply differentiated in their behaviour towards diphenylketen. The *cis*-forms react immediately at room temperature, whereas the same adducts are obtained from *trans*-isomerides only at high temperatures. The adducts are dimethylenedi-imine derivatives. The reactions with *cis*- and *trans-p*-chlorobenzenediazocyanide are also described.

In Parts I—III (III, J., 1939, 1315) the preparation of hitherto unknown isomerides of numerous azo-compounds by the chromatographing of irradiated solutions of the normal forms was described. The labile isomeride of azobenzene had been shown to have the *cis*-structure and, by analogy, the other isomerides were regarded as *cis*-isomerides of the normal *trans*-compounds; their ultra-violet absorption spectra confirmed this relationship. We then sought to differentiate the isomerides chemically.

Hartley (J., 1938, 642) mentions the unexpected behaviour of *cis*-azobenzene in concentrated hydrochloric acid, but this did not provide the significant differentiation we were seeking. Oxidation of *cis*-azobenzene by the well-known method of Angeli with hydrogen peroxide in acetic acid was investigated, but reaction was slow at temperatures sufficiently low to preclude prior reversion to the *trans*-azo-compound; consequently the only product was normal and not *cis* azoxy-benzene. Again the addition of sulphite or an aromatic sulphinic acid (Hantzsch and Glogauer, *Ber.*, 1897, **30**, 2548) to the azo-group was of doubtful value, since the double linking is destroyed and the product would have afforded no clue to the configuration of the initial azo-compound. Attention was therefore turned to addition reactions of the type:

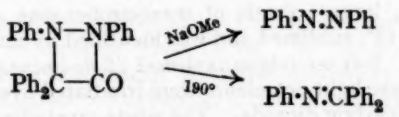


Here the *cis*-modification with a configuration approximating to that about to be assumed in the final adduct would be expected to react more rapidly than the *trans*-form.

Experiments to add (*a*) maleic anhydride, (*b*) diazoacetic ester, or (*c*) *as*.-diphenylethylene to *cis*- and *trans*-azo-compounds under conditions where these configurations would be retained were without useful result. Diazoacetic ester (Müller, *Ber.*, 1914, **47**, 3001) and diphenylethylene (Ingold and Weaver, J., 1925, **127**, 378) react readily with azodicarboxylic ester to give cyclic adducts, but do not react under mild conditions with purely aromatic *cis*- or *trans*-azo-compounds. More satisfactory was the reaction with diphenylketen. Staudinger ("Die Ketene," 1912, p. 91) mentions that reaction between diphenylketen and azo-compounds had been observed when they were heated together at 150° for several hours. Neither the preparative methods nor the products are described in any detail. Ingold and Weaver (*loc. cit.*) later obtained products from diphenylketen and azodicarboxylic ester or phenylazocarboxylic ester and showed that the adducts with one molecule of each of the reactants contained four-membered rings (I). We confirmed Staudinger's brief report and obtained a small amount of an *adduct* from *trans*-azobenzene and diphenylketen only after heating at 125—130° for 24 hours. However, when *cis*-azobenzene was added to diphenylketen at room temperature, reaction was vigorous with evolution of much heat. Even in light petroleum solution at room temperature reaction was rapid and the colour of the solution faded almost instantaneously. The product was the same as that obtained from the *trans*-isomeride at a high temperature. Irradiation of a light petroleum solution of *trans*-azobenzene containing diphenylketen provided a third and more convenient route to the same compound; clearly the *cis*-isomeride reacts immediately it is formed by irradiation.

$R\cdot N(-N\cdot CO_2Et)-CPh_2-CO$
(I, R = CO_2Et or Ph.)

Analysis showed that this product contained one molecule of each of the reactants. The adduct was stable to cold alcoholic alkali, but on warming with a dilute solution of sodium methoxide an excellent yield of azobenzene was obtained. At temperatures below its melting point (175°) the adduct was indefinitely stable, but at a slightly higher temperature decomposition occurred and by sublimation in a vacuum azobenzene and benzophenoneanil were obtained. These facts indicated a dimethylenedi-imine structure for the

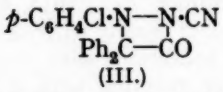


adduct (II) as envisaged by Staudinger; this structure is similar to that of the compounds obtained by Ingold and Weaver. Exactly similar adducts were obtained from *m*- and

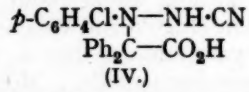
p-azotoluene. As before, when the *cis*-form was used, addition was rapid at room temperature, whereas when the *trans*-compound was used, high temperature was necessary; irradiation of the *trans*-form with diphenylketen again provided a convenient route to the same adducts.

Failure to isolate some *cis*-azo-compounds must, at least in some cases, mean that reversion to the *trans*-form is so rapid as to make isolation impossible; it is not surprising, therefore, that some such compounds (*o*-azotoluene, azonaphthalenes) yielded keten adducts by irradiation of solutions of the reactants as readily as those compounds which afforded more stable *cis*-modifications. On the other hand, the remarkable reactivity of such new azo-forms as have been isolated is regarded as very strong evidence of their *cis*-structure. It is unfortunate that this differentiating addition reaction cannot be used with all azo-compounds without involving further complications. Diphenylketen reacts with the substituent group of, for example, amino- and hydroxy-azo-compounds which cannot be examined by the chromatographic method. Thus *p*-aminoazobenzene yielded p-*diphenylacetamidoazobenzene*, so that examination by this means of the ability of aminoazobenzene to assume a *cis*-configuration is impossible.

This very great difference in reactivity suggested that other pairs of compounds containing *cis*- and *trans*-N : N linkages might show similar differences. *cis*- and *trans*-*p*-Chlorobenzenediazocyanide (Le Fèvre and Vine, J., 1938, 436) both reacted readily with diphenylketen in light petroleum; the same colourless *adduct*, m. p. 121°, was obtained from both compounds, although on one occasion the *cis*-cyanide afforded an isomeric adduct, m. p. 266°. These are provisionally regarded as the dimethylenedi-imine compounds formed by addition across the azo-linkage. The "normal" compound, m. p. 121°, is, in conformity with Ingold and Weaver's compounds, formulated as (III). Mild treatment



(III.)



(IV.)

with caustic alkali converted it into the *acid* (IV) (cf. Ingold and Weaver, *loc. cit.*); the latter was, however, unlike Ingold and Weaver's compound, not recyclised by treatment with acetyl chloride but was converted into another compound the nature of which was not fully investigated; it was not the acid chloride of (IV) or its *N*-acetyl derivative. The similar behaviour of the *cis*- and *trans*-cyanides indicates that the present differentiation between *cis*- and *trans*-azo-isomerides is to be expected only among otherwise unreactive aromatic azo-compounds.

Experimental.

4-*Keto*-1 : 2 : 3 : 3-*tetraphenyldimethylene*-1 : 2-*di-imine*.—(*a*) *trans*-Azobenzene (4 g.) was heated with diphenylketen (5 g.) in an atmosphere of carbon dioxide at 125—130° for 42 hours. The dark melt was digested with light petroleum, and the residual orange oil stirred with methanol. The pale yellow *adduct*, recrystallised from ethyl acetate, formed white needles (1·4 g.), m. p. 175° (Found : N, 7·6. $C_{26}H_{20}ON_2$ requires N, 7·5%). (*b*) *cis*-Azobenzene (0·5 g.) was treated with diphenylketen (0·6 g.) in light petroleum. The mixture reacted rapidly, but was kept overnight; the product, identical with that obtained in (*a*), was then filtered off and crystallised from ethyl acetate (0·4 g.). (*c*) Equimolecular quantities of diphenylketen and *trans*-azobenzene in light petroleum were irradiated before a mercury vapour lamp until the solution was bleached to pale yellow, The yellow oil which had separated was stirred with methanol; the adduct, identical with that obtained in (*a*) and (*b*), then solidified.

(i) The adduct (1 g.) was refluxed with 10% sodium methoxide in methanol (90 c.c.). After 30 minutes the solution was diluted with water and extracted with ether to give *trans*-azobenzene (0·32 g.). (ii) The adduct (0·3 g.) was heated at 190° for 1 hour. When the residual oil was heated at 60°/0·002 mm., large crystals of *trans*-azobenzene sublimed. At 100°/0·002 mm. benzophenoneanil, m. p. 112°, sublimed and was identified by mixed melting point.

4-*Keto*-3 : 3-*diphenyl*-1 : 2-*di*-*o*-*tolyldimethylene*-1 : 2-*di-imine*.—*o*-Azotoluene (1 g.) and diphenylketen (1·1 g.) in pure light petroleum were irradiated overnight before a mercury vapour lamp in an atmosphere of carbon dioxide. The white crystalline precipitate was recrystallised from ethyl acetate to give soft white needles (0·8 g.), m. p. 162° (Found : N, 7·2. $C_{28}H_{24}ON_2$ requires N, 7·0%).

*4-Keto-3 : 3-diphenyl-1 : 2-di-m-tolyldimethylene-1 : 2-di-imine.—cis-m-*Azotoluene (0·4 g.) and diphenylketen (0·6 g.) were mixed in light petroleum solution: the colour faded almost immediately. The petroleum was evaporated, and the residual oil dissolved in the minimum quantity of methanol. On standing, the *di-imine* was deposited; it was recrystallised from ethyl acetate (0·15 g.), m. p. 118° (Found: N, 7·1. $C_{28}H_{24}ON_2$ requires N, 7·0%). The same compound (0·75 g.) was obtained by irradiating *trans-m*-azotoluene (0·5 g.) with diphenylketen (0·6 g.) in light petroleum or, in very small yield, by heating the reactants in absence of solvent.

*4-Keto-3 : 3-diphenyl-1 : 2-di-p-tolyldimethylene-1 : 2-di-imine.—cis-p-*Azotoluene (0·3 g.) and diphenylketen (0·4 g.) were mixed in light petroleum. Reaction was rapid and a part (50 mg.) of the product separated at once. A further 0·5 g. was obtained by evaporating the mother-liquor and cooling the residue. The *di-imine* crystallised from ethyl acetate in white needles, m. p. 172° (Found: N, 7·1. $C_{28}H_{24}ON_2$ requires N, 7·0%). The same compound (0·1 g.) was obtained by irradiating *trans*-azotoluene (0·5 g.) and diphenylketen in light petroleum.

4-Keto-3 : 3-diphenyl-1 : 2-di-β-naphthyldimethylene-1 : 2-di-imine.—β-Azonaphthalene (0·5 g.) in 20 c.c. of benzene–light petroleum was treated with diphenylketen (0·4 g.), and the solution irradiated overnight. More petroleum was then added, precipitating a light yellow granular solid. The *di-imine* recrystallised from ethyl acetate in small colourless cubes (75 mg.), m. p. 222° (Found: N, 5·7. $C_{34}H_{24}ON_2$ requires N, 5·9%).

p-*Diphenylacetamidoazobenzene.—p-*Aminoazobenzene was treated with an equal weight of diphenylketen in benzene. After 12 hours, the solid was filtered off and recrystallised from benzene, forming light yellow-brown plates, m. p. 194° (Found: N, 10·4. $C_{26}H_{21}ON_3$ requires N, 10·6%). The same compound was obtained from *p*-aminoazobenzene and diphenylacetyl chloride.

*4-Keto-1-cyano-2-p-chlorophenyl-3 : 3-diphenyldimethylene-1 : 2-di-imine. — cis-p-*Chlorobenzenediazocyanide (1 g.) in light petroleum (15 c.c.) was added to diphenylketen (1 g.), also in light petroleum. Most of the colour was discharged at once and scratching caused the *di-imine* to separate (1·5 g.). Recrystallised from ethanol, it formed needles, m. p. 121° (Found: N, 11·4. $C_{21}H_{14}ON_3Cl$ requires N, 11·7%). When *trans-p-*chlorobenzenediazocyanide and diphenylketen were treated in the same manner, reaction was slower; small white needles began to separate after 30 minutes and the colour was practically discharged after 2 days. The product was identical with that obtained from the *cis*-cyanide. On one occasion the *cis*-cyanide afforded a product (Found: N, 11·8%), which crystallised from ethanol in white needles, m. p. 266°, but this preparation could not be repeated. The di-imine (1 g.), m. p. 121°, was refluxed for 1 hour with ethanol (20 c.c.) and 10% aqueous sodium hydroxide (5 c.c.). The solution was acidified, and the oil so obtained extracted with chloroform. The extract was dried and on evaporation deposited white cubes of *α-β′-cyano-α′-p-chlorophenylhydrazinodiphenylacetic acid*; this crystallised from ethanol in small white prisms, m. p. 288° (decomp.) (Found: N, 11·5. $C_{21}H_{16}O_2N_3Cl$ requires N, 11·5%). The compound was soluble in cold alkali, but no ammonia was evolved on short boiling.

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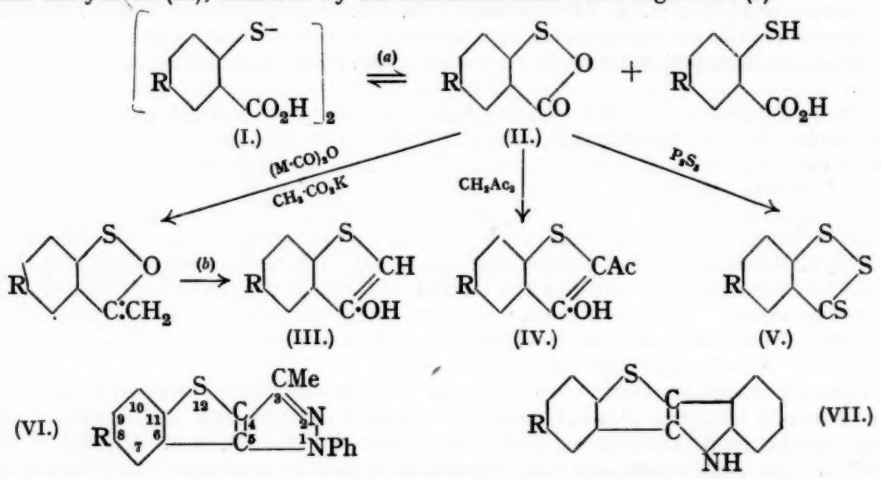
41. *The Dismutation of Some Disulphides. Part IV.*

By F. S. FOWKES and E. W. MCCLELLAND.

It is shown that chlorine in the para-position to sulphur decreases the tendency of a 2 : 2′-dithiobenzoic acid to undergo dismutation. In consequence 5 : 5′-dichloro-2 : 2′-dithiobenzoic acid reacts less readily than the non-chlorinated disulphide with acetylacetone in sulphuric acid but yields similar products, *viz.*, hydroxythionaphthens. The effect of chlorine as a substituent on the reactivity of these hydroxythionaphthens has been investigated. 2 : 2′-Dithiobenzoic acid undergoes dismutation in neutral media.

It has been suggested (Part II; D'Silva and McClelland, J., 1932, 2883) that the formation of thionaphthens in the reaction of 2 : 2′-dithiobenzoic acid with acetic anhydride and potassium acetate is dependent on the dismutation (*a*) of the disulphide and reaction of the sulphenic anhydride (II), followed by the intramolecular rearrangement (*b*).



5 : 5′-Dichloro-2 : 2′-dithiobenzoic acid (I; R = Cl) reacts with acetic anhydride and potassium acetate to give *5-chloro-3-hydroxy-2-acetyl-1-thionaphthen* (IV; R = Cl) and *5-chloro-3-acetoxy-1-thionaphthen* (III; R = Cl, OAc instead of OH). The dichlorodisulphide reacts less readily than the non-chlorinated disulphide, for 2 : 2′-dithiobenzoic acid (I; R = H) yields the thionaphthens when heated with the reactants at 120—125° for 2 hours, whereas 5 : 5′-dichloro-2 : 2′-dithiobenzoic acid requires heating at 130° for 4 hours with the reactants, little or no reaction taking place under the milder conditions effective for the non-chlorinated disulphide. It is evident that chlorine in the para-position to sulphur depresses the tendency of the disulphide to dismutation.

2 : 2′-Dithiobenzoic acid reacts with acetylacetone in sulphuric acid to give 3-hydroxy-2-acetyl-1-thionaphthen (Smiles and McClelland, J., 1921, **119**, 1810). The formation of the hydroxythionaphthen was attributed to condensation of the acetylacetone with the sulphenic acid formed by fission of 2 : 2′-dithiobenzoic acid in sulphuric acid. It seems probable that condensations of this type may be dependent on dismutation of the disulphide and that the sulphenic anhydride (II) and not the sulphenic acid may be the reactive intermediate.

5 : 5′-Dichloro-2 : 2′-dithiobenzoic acid also reacts with acetylacetone in presence of sulphuric acid to give 5-chloro-3-hydroxy-2-acetyl-1-thionaphthen (IV; R = Cl). The reaction proceeds less readily than with 2 : 2′-dithiobenzoic acid, thus supporting the conclusion that chlorine in the para-position to sulphur decreases the tendency to dismutation. The effect of chlorine in decreasing the tendency to dismutation suggests that chlorine in the para-position to sulphur partly neutralises the tendency of a carbonyl group in the ortho-position to sulphur to promote a positive charge on the sulphur atom, thereby rendering the sulphur atom in a chloro-compound less positive in character than in a corresponding unsubstituted compound. This would have the effect of decreasing the stability of the S–O link in the dismutation product (II) and therefore decrease the tendency to dismutation.

Comparison of the chlorohydroxythionaphthens with the unsubstituted hydroxythionaphthens shows that chlorine substitution has no marked effect on their reactivity; *e.g.*, 5-chloro-3-hydroxy-2-acetyl-1-thionaphthen readily gives the *chlorothionaphthenopyrazole* (VI; R = Cl) and 5-chloro-3-hydroxy-1-thionaphthen yields the *chlorothionaphthindole* (VII; R = Cl), with the same facility as the corresponding unsubstituted hydroxythionaphthens (compare Barry and McClelland, J., 1935, 471; McClelland and D'Silva, J., 1932, 227). Chlorine, however, does exert some effect on the heterocyclic nucleus, since

the chloro-compounds are not so readily oxidised to the thioindigotin as the unsubstituted compounds. It has been recorded (Smiles and Cohen, J., 1930, 411) that the 1 : 1-dioxide of 3-hydroxy-2-acetyl-1-thionaphthen cannot be obtained by direct oxidation with hydrogen peroxide owing to the formation of thioindigotin, and this has been confirmed. In contrast 5-chloro-3-hydroxy-2-acetyl-1-thionaphthen (IV; R = Cl) is oxidised with hydrogen peroxide under mild conditions to the 1 : 1-*dioxide* (IV; R = Cl, SO_2 instead of S). Similarly 5-chloro-3-acetoxy-1-thionaphthen (III; R = Cl, OAc instead of OH) is oxidised to the 1 : 1-*dioxide* (III; R = Cl, SO_2 instead of S, OAc instead of OH); more vigorous oxidation yields the deacetylated 1 : 1-*dioxide*, which gives a *hydrazone* resistant to indolisation (compare McClelland and D'Silva, J., 1932, 227). The *acetyl* derivative of 5-chloro-3-hydroxy-2-acetyl-1-thionaphthen appears to be more resistant to hydrolysis than the *acetyl* derivative of the corresponding non-chlorinated compound.

2 : 2′-Dithiobenzoic acid reacts with phosphorus pentasulphide in xylene to give 2 : 3-dithiosulphindene (V; R = H), which might be expected to result from the action of phosphorus pentasulphide on the sulphenic anhydride (II). The formation of 2 : 3-dithiosulphindene from 2 : 2′-dithiobenzoic acid supports the dismutation hypothesis, and suggests that 2 : 2′-dithiobenzoic acid undergoes dismutation in neutral as well as in acid media.

Experimental.

Reaction of 5 : 5′-Dichloro-2 : 2′-dithiobenzoic Acid with Acetic Anhydride and Potassium Acetate.—The acid (Hart, McClelland, and Fowkes, J., 1938, 2114) (1 g.) together with potassium acetate (1·25 g.) and acetic anhydride (12 c.c.) was heated at 130° for 4 hours. The mixture was poured into water, heated at 100° and distilled in steam. The distillate was extracted with ether, and the ethereal extract washed with 2N-sodium hydroxide. Acidification of the alkaline washings precipitated 5-chloro-3-hydroxy-2-acetyl-1-thionaphthen (0·05 g.). Evaporation of the ethereal extract gave 5-*chloro*-3-*acetoxy*-1-*thionaphthen* (0·2 g.), m. p. 67° (Found: C, 53·0; H, 3·2; S, 14·2. $C_{10}H_7O_2ClS$ requires C, 53·1; H, 3·1; S, 14·2%), which on hydrolysis gave 5-chloro-3-hydroxy-1-thionaphthen. The residue from the steam-distillation was unchanged starting material. At 125° little reaction resulted in 2 hours.

5-*Chloro*-3-*hydroxy*-2-*acetyl*-1-*thionaphthen.*—Acetylacetone (0·56 c.c.) was added portionwise during 1 hour to a well-stirred suspension of 5 : 5′-dichloro-2 : 2′-dithiobenzoic acid (1 g.) in concentrated sulphuric acid (8 c.c.) kept at 50—55°. The mixture was kept for 40 minutes at 50—55°, then poured on ice, and the solid material collected, washed with water, and extracted with 2N-sodium hydroxide. The alkaline extract was filtered and acidified. The precipitate crystallised from alcohol (charcoal) in yellow plates (0·75 g.), m. p. 166° (Found: C, 52·8; H, 2·9; S, 14·1. $C_{10}H_7O_2ClS$ requires C, 53·0; H, 3·1; S, 14·2%). 5-*Chloro*-3-*hydroxy*-2-*acetyl*-1-*thionaphthen* gives an olive-green coloration with alcoholic ferric chloride and is oxidised by warm alkaline potassium ferricyanide to the corresponding thioindigotin.

5-Chloro-3-hydroxy-2-acetyl-1-thionaphthen (1 g.) was refluxed in toluene (20 c.c.) containing acetic anhydride (4 c.c.) and a trace of pyridine for 6 hours. The *acetyl* derivative crystallised in colourless needles, m. p. 132°, on addition of light petroleum to the cooled solution (Found: C, 53·4; H, 3·1. $C_{12}H_9O_3ClS$ requires C, 53·6; H, 3·3%). It gave no coloration with alcoholic ferric chloride and was deacetylated to 5-chloro-3-hydroxy-2-acetyl-1-thionaphthen by refluxing with 2N-sulphuric acid for 1½ hours. 3-*Acetoxy*-2-*acetyl*-1-*thionaphthen*, prepared in a similar way, had m. p. 127° (Found: C, 61·6; H, 4·1. $C_{12}H_{10}O_3S$ requires C, 61·5; H, 4·1%), and was deacetylated to 3-hydroxy-2-acetyl-1-thionaphthen in 30 minutes under similar conditions.

8-*Chloro*-1-*phenyl*-3-*methyl*-4 : 5-*thionaphthenopyrazole.*—A solution of 5-chloro-3-hydroxy-2-acetyl-1-thionaphthen (1 g.) and phenylhydrazine (1·45 g.) in benzene was refluxed for 3 hours. The *hydrazone*, which separated overnight, crystallised from benzene in yellow prisms, m. p. 162° (Found: C, 60·5; H, 4·2. $C_{16}H_{13}ON_2ClS$ requires C, 60·7; H, 4·1%). A solution of the hydrazone (0·1 g.) in alcohol containing a drop of concentrated sulphuric acid was refluxed for 30 minutes. The solution was diluted with water and the material, precipitated on cooling, was collected and washed with alkali and acid. It crystallised from alcohol in colourless needles, m. p. 135°(Found: C, 64·2; H, 4·1. $C_{16}H_{11}N_2ClS$ requires C, 64·3; H, 3·7%).

5-*Chloro*-3-*hydroxy*-2-*acetyl*-1-*thionaphthen* 1 : 1-*Dioxide.*—Finely ground 5-chloro-3-hydroxy-2-acetyl-1-thionaphthen (0·5 g.) was suspended in acetic acid (5 c.c.) and hydrogen peroxide (0·6 c.c., 90—100 vol.) was added to the mixture, which was left for 3 days. The required

material, together with a small amount of the thioindigotin, separated. It crystallised from benzene–petroleum (charcoal) in colourless plates, m. p. 265° (Found: C, 46·7; H, 2·8. $C_{16}H_7O_4ClS$ requires C, 46·4; H, 2·7%).

10-*Chlorothionaphthindole.*—A solution of 5-chloro-3-hydroxy-1-thionaphthen (0·5 g.) and phenylhydrazine (0·3 g.) in acetic acid was heated at 100° for 35 minutes. The product which separated was washed with a little alcohol; it crystallised from acetic acid in colourless plates, m. p. 222° (Found: C, 65·05; H, 3·4. $C_{14}H_8NClS$ requires C, 65·25; H, 3·1%). It gave a blue coloration with isatin in sulphuric acid. It was also obtained in a similar way from 5-chloro-3-acetoxy-1-thionaphthen.

5-*Chloro*-3-*acetoxy*-1-*thionaphthen* 1 : 1-*Dioxide.*—Hydrogen peroxide (0·5 c.c., 90—100 vol.) was added to a suspension of 5-chloro-3-acetoxy-1-thionaphthen (0·3 g.) in acetic acid (2 c.c.), and the mixture kept for 4½ days with frequent shaking. The product (0·15 g.), which separated, crystallised from benzene–petroleum (charcoal) in colourless prisms, m. p. 164° (Found: C, 46·7; H, 2·8. $C_{16}H_7O_4ClS$ requires C, 46·4; H, 2·7%).

5-*Chloro*-3-*hydroxy*-1-*thionaphthen* 1 : 1-*Dioxide.*—A solution of 5-chloro-3-acetoxy-1-thionaphthen (1 g.) in acetic acid (12 c.c.) and hydrogen peroxide (6 c.c., 90—100 vol.) was heated at 100° for 1 hour, and water added. The material (0·5 g.), which separated on cooling, crystallised from benzene–petroleum in colourless needles, m. p. 194° (Found: C, 44·2; H, 2·3. $C_8H_5O_3ClS$ requires C, 44·3; H, 2·3%). 5-*Chloro*-3-*hydroxy*-1-*thionaphthen* 1 : 1-*dioxide phenylhydrazone*, obtained by heating the above material (1 mol.) in glacial acetic acid with phenylhydrazine (3 mols.), crystallised from acetic acid in yellow needles, m. p. 290—292° (Found: C, 54·6; N, 3·7. $C_{14}H_{11}O_2N_2ClS$ requires C, 54·8; H, 3·6%). The hydrazone resisted attempts to indolise it.

Reaction of 2 : 2′-*Dithiobenzoic Acid with Phosphorus Pentasulphide.*—2 : 2′-Dithiobenzoic acid (30 g.) in xylene (1 l.) and phosphorus pentasulphide (30 g.) were refluxed with stirring for 6 hours. After filtration the xylene was removed in steam and the residual oily material was heated at 100° for some time to remove traces of water and xylene. 2 : 3-Dithiosulphindene was obtained from the product by crystallisation from alcohol. Yield, 75%.

The authors are indebted to the Department of Scientific and Industrial Research for a grant to one of them (F. S. F.).

KING'S COLLEGE, LONDON. [*Received, March 13th,* 1941.]

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42. *The Synthesis of* N-*Trimethylglycylcholine.*

By THOMAS S. WORK.

Trimethylglycylcholine has been synthesised by the condensation of trimethylamine and a halogenoethyl ester of a halogenoacetic acid.

DUDLEY (J., 1921, **119**, 1256), in the hope of obtaining bases of pharmacological interest, began a study of amino-acid esters of choline. Glycylcholine was prepared, but the subject was not further pursued. It was suggested to me by Sir Henry Dale, P.R.S., that a completely methylated glycylcholine might possess the high physiological activity which Dudley sought.

Trimethylglycylcholine was readily obtained in a single step by heating a halogenoethyl ester of a halogenoacetic acid with anhydrous trimethylamine in a sealed tube:

$$Hal{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}CH_2Hal + NMe_3 \longrightarrow Hal{\cdot}NMe_3{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}CH_2{\cdot}NMe_3{\cdot}Hal$$

The first synthetic attempt was made with β-*bromoethyl chloroacetate.* The bromoethyl ester was used in preference to the simpler chloroethyl ester in an attempt to make the halogens equally reactive. The yield by this method was poor, as the resultant mixture of chlorides and bromides was difficult to purify and only *trimethylglycylcholine dibromide* could be isolated. Subsequent preparations showed this precaution to be unnecessary, and yields up to 70% were obtained by using β-bromoethyl bromoacetate.

As analysis of *trimethylglycylcholine picrate* would not readily distinguish it from choline picrate, and as the melting points of the two picrates were very similar and showed very

little depression on mixing, it was found desirable to confirm the structure of the synthetic product by degradation. When trimethylglycylcholine dibromide was shaken with silver oxide in water, it decomposed immediately, and after removal of silver salts betaine was readily isolated from the filtrate. The synthetic ester was also readily distinguished from choline by the properties of its *platinichloride*, which was very much less soluble than choline platinichloride and did not show the dimorphism characteristic of the choline salt.

Pharmacological tests on trimethylglycylcholine dibromide by Dr. F. C. MacIntosh, to whom I wish to express my thanks, showed that it possessed an extremely weak muscarine-like activity and no perceptible curare-like, nicotine-like or eserine-like activity. It was, like glycylcholine, pharmacologically rather inert.

Experimental.

β-*Bromoethyl Chloroacetate.*—Chloroacetyl chloride (22·6 g.) was added slowly to ethylene bromohydrin (28·0 g.) so that the temperature did not rise above 50°. The product was poured into ether, washed thoroughly with water, dried, and distilled. The fraction, b. p. 112—114°/22 mm., was collected (Found: C, 24·1; H, 3·1. $C_4H_6O_2ClBr$ requires C, 23·8; H, 3·0%); yield, 90%.

β-Chloroethyl chloroacetate, b. p. 101°/32 mm., and β-bromoethyl bromoacetate, b. p. 118°/16 mm., were prepared in the same way (cf. Henry, *Bull. Soc. chim.*, 1884, **42**, 260; Vorländer, *Annalen*, 1894, **280**, 198) in approximately the same yield.

Trimethylglycylcholine Dibromide.—β-Bromoethyl chloroacetate (20·1 g.) was sealed in a thin-walled test-tube and placed inside a Carius tube cooled in ice-salt. Cold anhydrous trimethylamine (18 c.c.) and cooled dry benzene (20 c.c.) were added, and the tube sealed as rapidly as possible; the thin inner tube was broken, and the contents thoroughly mixed. The temperature rose rapidly and crystals separated. When the initial reaction had subsided, the tube was heated at 100° for 8 hours. The solid white cake produced was broken up, washed with dry benzene, and dissolved in alcohol. A small quantity of residual insoluble material was removed and found to be betaine bromide. After several days a crystalline crust separated from the alcohol and after five recrystallisations from alcohol it was obtained in white rosettes of needles, m. p. 238°. Analysis indicated that this least soluble fraction was *trimethylglycylcholine dibromide* (Found: Br, 43·5. $C_{10}H_{24}O_2N_2Br_2$ requires Br, 44·0%). The dibromide, treated with aqueous sodium picrate, gave a *dipicrate*, which crystallised readily from aqueous alcohol in long needles, m. p. 244° (Found: C, 39·4; H, 4·5; N, 17·2. $C_{10}H_{24}O_2N_2,2C_6H_3O_7N_3$ requires C, 39·8; H, 4·5; N, 16·9%).

The alcoholic mother-liquor from the dibromide crystallisation was concentrated in the hope of obtaining the dichloride, but no crystalline material could be isolated. The yield of dibromide was about 15%. With gold chloride or platinic chloride in dilute hydrobromic acid the dibromide gave crystalline salts sparingly soluble in cold water. The gold salt crystallised in short reddish needles, m. p. about 250° (decomp.); the platinum salt crystallised in twinned prisms and melted over a range of 20° depending on the rate of heating.

A second preparation of trimethylglycylcholine dibromide carried out as described above, but using β-bromoethyl bromoacetate as starting material, gave a yield of 68% of pure dibromide.

Trimethylglycylcholine Dichloride.—β-Chloroethyl chloroacetate (7·5 g.) reacted with trimethylamine (5·63 g.) in 16 hours by the above process, but difficulty was experienced in purifying the product as the dichloride. After removal of a small quantity of betaine chloride, trimethylglycylcholine picrate was isolated, m. p. 244°, identical with the picrate obtained above.

Trimethylglycylcholine Platinichloride.—Trimethylglycylcholine chloride gave with platinic chloride a yellow crystalline precipitate sparingly soluble in cold water. The platinichloride was crystallised from hot water and from 50% aqueous alcohol, but did not show the dimorphism characteristic of choline platinichloride and crystallised from both solvents in trigonal prisms containing no water of crystallisation; these melted over a range of about 20° with variation in the rate of heating (Found: Pt, 31·2. $C_{10}H_{24}O_2N_2,PtCl_6$ requires Pt, 31·8%).

National Institute for Medical Research,
London, N.W. 3.

[*Received, March 19th*, 1941.]

NOTE.

The Preparation of 4-Acetamido-2-hydroxyphenylarsenoxide. By MONTAGUE A. PHILLIPS.

4-ACETAMIDO-2-HYDROXYPHENYLARSENOXIDE has hitherto been obtained from the corresponding arsonic acid by reduction with sulphurous acid (Cohen, King, and Strangeways, J., 1932, 2509), but the yield recorded by these authors could not be obtained in these laboratories and never exceeded 10%. The product was difficult to purify and considerable amounts of inorganic arsenic compounds were found in mother-liquors. This oxide has now been obtained in good yield by the following convenient method.

p-*Benzarsenious Acid* (compare Mann, J., 1932, 966).—*p*-Benzarsonic acid (50 g.) was dissolved in concentrated hydrochloric acid (500 c.c.) by boiling. To the solution, cooled to 40°, was added 10% potassium iodide solution (10 c.c.) and sulphur dioxide was passed for 2 hours. The *p*-carboxyphenyldichloroarsine so formed was collected, washed with concentrated hydrochloric acid, and drained on a porous tile. Solution in water (600 c.c.) by means of the requisite amount of 25% sodium hydroxide solution and precipitation by 2N-sulphuric acid after filtration (just acid to Congo-red) gave *p*-benzarsenious acid (39 g., 83% of the theoretical amount) (Found: As, 32·5. Calc.: As, 32·6%).

Biscarboxymethyl 4-Acetamido-2-hydroxyphenylthioarsinite.—Barium thiolacetate (crude, 105 g., corresponding to 35 g. of thiolacetic acid) was dissolved in water (240 c.c.) by means of concentrated hydrochloric acid (140 c.c.). Sufficient 2N-sulphuric acid was added completely to remove the metal as sulphate, and after addition of charcoal (5 g.) the liquid was filtered. The solids were washed with water (twice with 50 c.c.), and the filtrate neutralised with cooling with 25% sodium hydroxide solution. To the solution of sodium thiolacetate so obtained was added 4-acetamido-2-hydroxyphenylarsonic acid (24·5 g.), and the solution again adjusted to litmus with caustic soda solution. On stirring, solution ensued; the filtered solution (charcoal) was acidified to Congo-red with hydrochloric acid, the thioarsinite being precipitated as an oil which soon crystallised. Purified by reprecipitation of its solution in 2N-sodium hydroxide with hydrochloric acid, the pure *thioarsinite* was obtained in 90% yield, m. p. 160—161° (Found: As, 18·4. $C_{12}H_{14}O_6NS_2As$ requires As, 18·4%). This aryl thioarsinite (120 g.) was suspended in water (600 c.c.) and dissolved by means of sufficient 10% sodium hydroxide solution to give a solution neutral to litmus. A neutral solution of *p*-benzarsenious acid (65 g.) in water (600 c.c.) and 10% sodium hydroxide was similarly prepared and the solutions were mixed at 35°. After a few seconds delay, a crystalline precipitate of the arsenoxide was formed; this was collected, washed with water, and dried in a vacuum over sulphuric acid. It weighed 57 g. (73% of the theoretical amount) and had all the properties ascribed to it by Cohen, King, and Strangeways (*loc. cit.*) (Found: As, 29·9; N, 5·6. Calc. for hemihydrate: As, 30·0; N, 5·6%).

From the filtrate by acidification with hydrochloric acid was obtained crude biscarboxymethyl 4-carboxyphenylthioarsinite. Purified by reprecipitation of its solution in caustic alkali with mineral acid, it weighed 80 g. and melted at 176° alone or mixed with a preparation obtained from *p*-benzarsonic acid and thiolacetic acid by Barber's method (J., 1929, 1020). The above arsenoxide can also be obtained in the same yield by substituting the equivalent amount of bis-*o*-carboxyphenyl 4-acetamido-2-hydroxyphenylthioarsinite for the other arylthioarsinite in the above preparation. In neither case was any inorganic arsenic compound detected.

5-Acetamido-2-hydroxyphenylarsenoxide could not be obtained under the same conditions, no insoluble precipitate being formed.—RESEARCH LABORATORIES, MESSRS. MAY AND BAKER, LTD., DAGENHAM. [*Received, February 3rd*, 1941.]

THE HUNDREDTH ANNIVERSARY MEETING.

THE Annual General Meeting was held at Burlington House on Thursday, 3rd April, 1941, at 12 noon. The President, SIR ROBERT ROBINSON, F.R.S., occupied the Chair.

The notice convening the meeting was read and the President then said:

Before proceeding with the formal business of the meeting it will be appropriate to make reference to the fact, which is uppermost in our minds today, that the Chemical Society was founded in 1841. This is the hundredth Anniversary meeting. The present is no time for festive occasions, for reunions with our distinguished Honorary Fellows, for international intellectual co-operation generally, and certainly not for an organised Scientific Congress. Therefore the Council has decided to postpone our Centenary Celebrations, which must be compounded of all these elements, until after the war. Even then there will probably be an interval to allow for preparation. This decision has no negative qualities, but is a positive affirmation of our intention to organise as soon as possible an occasion worthy of the Society's splendid record and high position among the Academies of the world. Any feeling of disappointment arising from the inadequacy of our present action is therefore not warranted, and I am satisfied that the Council's views are endorsed by the great majority of Fellows of the Society.

We may, however, recall a few of the outstanding events relating to our foundation, very briefly, especially in view of the fact that Professor J. C. Philip, President-Elect, is compiling a detailed history of the Society and has already completed his account of the first thirty years.

The man who conceived the idea of forming a Chemical Society was Robert Warington, a chemist of distinction who later made important original contributions to the *Journal*. He was a member of the Mathematical Society of Spitalfields (founded in 1788), and it was in discussions with some fellow-members that the project was born.

Warington enlisted the support of influential chemists, among whom was certainly Thomas Graham, and a meeting was called after it had been ascertained by correspondence that the scheme was likely to receive enthusiastic support. The report dated 23rd February, 1841, shows that there were 77 original members, including W. Crum, C. Daubeny, E. Davy, Warren de la Rue, G. Fownes, W. R. Grove, H. Hennell, W. Herapath, T. C. Hope, G. D. Longstaff, W. H. Miller, T. Moody, F. Penny, Lyon Playfair, J. Stenhouse, T. Thomson, J. Tennant, and many other well-known names. The first officers were: President, Prof. Thos. Graham; Vice-Presidents, Prof. W. T. Brande, J. T. Cooper, Prof. J. E. Daniell, and R. Phillips; Treasurer, A. Aikin; Secretaries, R. Warington and E. F. Teschemacher.

The first scientific meeting was held on 13th April, and the first paper read was a translation of one by Liebig of Giessen on "The Preparation of Yellow Prussiate of Potash." There is much evidence of the very valuable support given by Liebig in the early years of the Society. At this meeting E. A. Parnell of University College, apparently not a member, read a paper "On the Formation of Mellon."

On 27th April a second meeting was held and a gift of five guineas from Dr. W. B. Leeson was acknowledged. This donation remained alone in the records for more than two years. A letter from Mr. Scanlan of Wolverhampton was read. It described flashes seen on crystallisation of strontium nitrate in the dark.

Other papers were read and appeared later in the "Memoirs." (Three volumes of "Memoirs and Proceedings" were succeeded by the *Quarterly Journal*.) A note by the President described an improved method of preparation of chlorates. He recommended the use of a mixture of slaked lime and potassium carbonate for the more economical use of chlorine. This is mentioned as an instance of the great interest taken in good preparative methods and in the industrial applications of chemistry.

At the meeting on 11th May the gift by Dr. Daubeny of his "Lectures on Agriculture" was acknowledged. The library at this time could probably have been housed on a single shelf. Papers read were by Professor William Gregory of Aberdeen on the preparation

of pure hydrochloric acid and by Liebig and Redtenbacher on the atomic weight of carbon. At this and at most succeeding meetings the election of new members and associates was announced. On 1st June Liebig was elected the first Foreign Member. Robert Bunsen was similarly honoured on 1st February, 1842, Joseph Redtenbacher of Prague on 14th March, 1842, and A. W. Hofmann in 1845.

After the vacation, on 2nd November, a letter from Dumas on the analysis of air was read. On 7th December a paper by Bunsen of Marburg was read; it described new caccodyl compounds containing platinum. On this occasion Warington read a paper on the preparation of chromic acid. On 4th January, 1842, the name of Michael Faraday appears among those of the new members, and on 15th March the election of Edward Schunck was announced. James P. Joule became a member in 1844.

The first Anniversary meeting was held on 30th March, 1842. Faraday became a Vice-President and George Fownes joined R. Warington as Secretary; E. F. Teschemacher became Foreign Secretary. The Council's Report was hopeful, if a little austere in places. It was stated that the Society was induced to leave its first home in the Rooms of the Society of Arts, John Street, Adelphi, because of some anticipated inconvenience in the performance of experiments. The Council was by no means satisfied with the new quarters in the Western Literary and Scientific Institute, as it had no Council Room and no library facilities or space for the preservation of specimens. It appears that the member's subscription was £2, and one composition of £10 was paid. On this first occasion the Auditors' report agreed with the Treasurer's Balance Sheet within the limits of experimental error.

The progress of the Society after its first year cannot be followed here because the subject is too large. We moved back to John Street, rejected a suggestion of Kensington Gore because of the inconvenience of the suburbs, then went to Cavendish Square, and a little time later to Burlington House. The number of members grew as follows: 1843, 77 London, 57 country members and 3 Foreign members; 1844, the numbers were 78, 71, and 4, respectively, as well as 15 associates; 1845, 88 London members and 90 country members. This shows how quickly the Society became national in scope.

And so from strength to strength; the membership, the number and even the importance of original communications increased rapidly; the library, at first a mere nucleus, developed until the problem was not how to secure books but how to house them. Abstracts, Memorial Lectures, a list of Foreign members that could be used as headings for a History of Chemistry, Annual Reports, Research Grants, the Scheme of Co-operation—no attempt can be made today to appraise this great achievement. But finally we may be sure that the centenary will be celebrated in no spirit of self-satisfaction; the Chemical Society will not rest on its laurels, and the glories of the next hundred years will equal those of the past. This is the faith in which the pioneers of 1841 would wish us to persevere.

The PRESIDENT then referred to the fact that he had received the following letter from the Chancellor of the Duchy of Lancaster.

From the Chancellor of the Duchy of Lancaster.

55, *Whitehall*,
S.W. 1.
24th March, 1941.

DEAR SIR ROBERT,

The Scientific Advisory Committee of the War Cabinet, of which I am Chairman, were much interested in the account which you gave them the other day of the work of the Advisory Research Council set up by the Chemical Society.

You explained to the Committee that the Council's object was to suggest to research workers in University Departments problems which they might usefully attack as volunteers, but which were not of sufficient urgency to warrant the expenditure of public funds. The Committee noted that more than 100 such problems had been taken up and were being actively pursued.

The Committee felt that voluntary work of this kind was of the greatest value as a

contribution to the national war effort and they invited me, as Chairman, to write and convey to you their appreciation of the work which the Advisory Research Council of the Chemical Society is doing. In order to strengthen the contacts between the Council and the Scientific activities of Government Departments, the Committee requested the Secretaries of the Department of Scientific and Industrial Research, of the Medical Research Council and of the Agricultural Research Council to refer to your Society any suitable problems that might come to their notice.

Yours sincerely,
(*Signed*) HANKEY.

Sir Robert Robinson, F.R.S., M.A.

It was agreed that the thanks of the Society be returned for this encouragement of the work of the Advisory Research Council.

The Report of Council for 1940 was presented, and the Senior Secretary, in introducing the general sections of the Report, referred to the launching of the new Co-operation Scheme, and recalled the great debt that it owed to Dr. Ellingham for his advocacy, and for the time and energy he had devoted, when Senior Secretary of the Society, to formulating a practicable basis of co-operation. He then spoke of the excellent work of the depleted office staff during the winter months, when the additional burden involved by the inauguration of the new scheme was superimposed upon the difficulties resulting from enemy action over London, and paid a tribute to Mr. Carr, the General Secretary, for the great part he had played in maintaining the normal services of the Society under trying conditions.

The Treasurer, who was then called upon by the PRESIDENT to deal with the accounts, said that he regarded the year 1940 as a transitional year, as in 1941 the new Scheme of Co-operation came into being. But for that the decrease in membership subscriptions of £305 15*s.* 2*d.* would have involved serious implications for the future. As, however, there were so far over 1300 chemists who had applied for membership of the three Chartered Bodies under the Scheme, and of these over 700 were not Fellows of the Chemical Society in 1940, he thought that they could face the future with confidence, even despite the year's deficit.

Turning to the Report of the Bureau of Chemical and Physiological Abstracts, he pointed out that the accounts for A III were now embodied in that report, and not in the accounts of the Society, since the Bureau was responsible for administering the A III Fund. He also stressed the importance of the renewal of the Agreement for the production of A III and the increased grants promised from contributing Societies. He mentioned that work on the Quinquennial Index was proceeding satisfactorily, the Author Index having been published during 1940, and the Subject Index was expected to be ready before the end of 1941.

He then drew attention to the creation of the Special Reserve Fund and to the fact that the deficit of £463 10*s.* 11*d.* shown in the General Purposes Account was due to the transfer thereto of £1100 on account of Publications and £200 on account of Library expenditure.

The effect of the last war on the cost of publications was shown in Table I.

TABLE I.

Cost of JOURNAL *and* ABSTRACTS, 1914, 1919, 1920, *and* 1921.

Year.	Gross cost.	Increase over 1914.	Sales.	Net cost.	Net increase over 1914.
	£	£	£	£	£
1914	5,833	—	1401	4432	—
1919	7,246	1413	1820	5426	994
1920	9,416	3579	2591	6821	2389
1921	11,524	5691	3100	8424	3992

These increased costs were due to the abnormal number of papers received for publication owing to the great influx of students to the Universities after the war, and to

the leeway in abstracting that had to be made up. As surpluses obtained during the war years were invested in the general funds of the Society, financial difficulties supervened in the post-war years.

A similar situation had arisen in this war, as was shown in Table II.

TABLE II.

Cost of JOURNAL *and* ABSTRACTS, 1939 *and* 1940.

Year.	Cost of production. *Journal.* £ s. d.	Cost of production. A I and A II. £ s. d.	Sales. *Journal.* £ s. d.	Sales. A I and A II. £ s. d.	Year.
1939	6651 13 0	5654 2 1	3250 16 5	2069 10 5	1939
1940	5839 3 4	4767 2 7	2768 6 2	1894 8 9	1940
Saving	812 9 8	886 19 6	482 10 3	175 1 8	Decrease
	Total saving £1699 9*s.* 2*d.*		£657 11*s.* 11*d.*	Total decrease.	
	Net saving £1041 17*s.* 3*d.*				

Since conditions might be expected to be not very different in the post-war years from those prevailing from 1919 onwards, the Council had decided to put £1100 to the Special Reserve Fund on account of publications.

Turning to the Library Account, he pointed out that a sum of £200 had been put to the Special Reserve Fund on account of books and binding, and it was anticipated that this would be sufficient to purchase books and periodicals not now obtainable in this country. The saving in expenditure on books, periodicals, and binding was much greater than this, viz. £384 11*s.* 11*d.*, but there were far fewer scientific and technical books being published during the war.

The Accounts and Balance Sheets therefore represented, as far as could be foreseen, the financial position of the Society at the present time, provision having been made for post-war eventualities.

The adoption of the Report of Council for 1940, including Statements of Accounts and Balance Sheets, was proposed by Professor F. J. Wilson, seconded by Dr. J. T. Hewitt, and carried unanimously.

The names of Fellows elected to vacancies on the Council were declared as follows:

President: Professor J. C. Philip.

Vice-Presidents, who have filled the Office of President: Professor P. F. Frankland, Professor G. G. Henderson, Sir Robert Robinson, Professor N. V. Sidgwick, Professor W. P. Wynne.

Elected Ordinary Members of Council:

Constituency I. South-East England.
Dr. H. J. Emeléus (London).
Dr. J. J. Fox (London).
Dr. B. C. Saunders (Cambridge).

Constituency IV. North-East England.
Professor J. M. Gulland (Nottingham).
Professor R. D. Haworth (Sheffield).

Constituency V. Scotland.
Professor G. F. Marrian (Edinburgh).

A vote of thanks to the Vice-Presidents, Treasurer, Honorary Secretaries, Council, and Committees for their services during the past year, proposed by Professor T. S. Moore and seconded by Dr. H. J. Emeléus, was carried unanimously, Professor F. M. Rowe making acknowledgment.

On the motion of Dr. F. S. Dainton, seconded by Mr. T. H. Reade, Messrs. W. B. Keen & Co., were appointed auditors for 1941.

The meeting was then adjourned.

A luncheon at which eighty Fellows and their guests were present was held at Kempinski's Restaurant, Swallow Street, at 1 p.m. At the conclusion of the luncheon, after the loyal toasts had been honoured, the President referred to the presence of Dr. J. B. Conant, President of Harvard University, and called on Professor N. V. Sidgwick to propose his health. This was acknowledged by Dr. Conant.

The toast of the newly elected President, Professor J. C. Philip, was proposed by Sir Robert Pickard and acknowledged by Professor Philip.

At 2.45 p.m. the meeting was resumed and the retiring President, Sir Robert Robinson, delivered his Presidential Address, entitled " The Mechanism of the Benzidine Rearrangement and some Related Topics." At its conclusion a vote of thanks to the President for his services in the Chair during the past two years and for his Address, with the request that he would allow the Address to be printed in the *Journal*, was proposed by Professor J. L. Simonsen and seconded by Dr. J. Kenyon. This was carried unanimously, and acknowledged by Sir Robert Robinson.

Professor J. C. Philip was then inducted into the Chair and spoke for a few minutes, expressing his appreciation of the honour that had been conferred on him.

REPORT OF COUNCIL, 1940.

The outstanding feature of the year has been the adoption by the Chemical Society, the Institute of Chemistry, and the Society of Chemical Industry of the new Scheme of Co-operation. This was approved after having been circulated to Fellows for their comments, and comes into effect on the 1st January, 1941. Whilst it is impossible to forecast the ultimate consequences of this step in co-operation, it can be predicted that many more chemists will be attracted by the joint membership concessions to participate in the work of the Society, and that with the aid of the Chemical Council it will be possible to improve the Publications, which for many years have suffered from financial restrictions. The inception of the Scheme has imposed much extra labour on the already depleted Staff of the Society, and the Council trust that Fellows will show forbearance while the initial difficulties are being overcome.

The Society will attain its Centenary in 1941, and it is the hope of the Council that this event will be celebrated appropriately when peace has been established. In the meantime the activities of the Society continue on a wartime scale. Both *Journal* and *Abstracts A* have diminished in size, but have continued to appear at monthly intervals.

The rooms of the Society have so far been fortunate in escaping serious air raid damage. Joint arrangements for firewatching have been made in co-operation with the other Societies occupying rooms in Burlington House, and it is believed that the measures taken have greatly reduced the danger from incendiary bombs.

I. FELLOWSHIP.

(1) *Fellowship Statistics.*

The number of Fellows on the 31st December, 1939, was 3773. During 1940, 153 Fellows were elected and 11 reinstated, the corresponding figures in 1939 being 186 and 15, respectively. The Society has lost 50 Fellows through death, 121 by resignation, and 71 by removal for non-payment of annual subscription, making a total loss of 242, as against 227 in 1939. The number of Fellows on the 31st December, 1940, therefore, was 3695, showing a decrease of 78.

The names of those Fellows to whom the Council have conveyed the congratulations of the Society on completing 60 and 50 years of Fellowship have appeared in the *Proceedings*. Among these is Professor Percy F. Frankland, President from 1911 to 1913.

(2) *Deaths.*

The Council deplore the loss of their distinguished Honorary Fellow, Sir Joseph J. Thomson, O.M., F.R.S., whose death took place on the 30th August. They have also to

mourn the loss of two Past-Presidents, Sir Gilbert T. Morgan and Sir Jocelyn F. Thorpe. Resolutions expressing the sympathy of the Council and recording their high appreciation of the services rendered by these Fellows to the Society have been passed and published in the *Proceedings*.

The Council are arranging for a Memorial Lecture to be given in honour of Sir J. J. Thomson, and for Obituary Notices of Sir Gilbert Morgan and Sir Jocelyn Thorpe to be published in the *Journal*.

II. PUBLICATIONS.

(1) *Journal.*

During the year 291 papers were received by the Society; of these 5 were declined.

In addition to Obituary Notices and reports on Atomic Weights, Isotopes, Inorganic Nomenclature, and the Annual General Meeting, the *Journal* for 1940, occupying 1576 pages, contains 297 memoirs (73 on General, Physical, and Inorganic Chemistry and 224 on Organic Chemistry), 15 notes, and 5 lectures, including the Presidential Address. The corresponding figures for 1939 are 1962 pages, 401 memoirs, 33 notes, and 4 lectures.

(2) *Abstracts.*

The report of the Bureau of Chemical and Physiological Abstracts for 1940 appears as Appendix A to this report.

As a measure of economy, the Council informed the Bureau that the cost of Abstracts A I and A II in 1940 must not exceed that for 1939, and that the number of pages should be at least 200 less in 1940 than in 1939. It has also been decided that a smaller type shall be used in 1941.

The original Agreement for the production of A III, which expired at the end of 1940, has been extended for a further period of three years, and the Society has increased its grant from £1300 to £1500 per annum.

During the year Dr. L. H. Lampitt was elected Chairman of the Bureau and Mr. F. P. Dunn Treasurer. It has also been decided that Miss M. Le Pla (Indexer) and her staff should be under the sole control of the Bureau.

(3) *Annual Reports.*

Volume XXXVI (1939) of the *Annual Reports on the Progress of Chemistry*, published in April, 1940, contained 419 pages compared with 410 in the preceding volume.

III. MEETINGS.

(1) *Scientific Meetings.*

The Society has held three Lectures in London. Owing to the intensification of War conditions, no meetings have been held in London since April.

The Council are gratified to record that 27 meetings were held outside London.

A complete list of these meetings is given in Appendix C.

(2) *Anniversary Meetings.*

The Anniversary Meetings of the Society were held in London on 4th April, 1940. These included Sir Robert Robinson's Presidential Address entitled "Some Aspects of the Chemotherapy of Tuberculosis. A Speculation regarding the Ring Structure of the Sterols and Related Substances," and the Sörensen Memorial Lecture by Professor E. K. Rideal. A full report of the meeting appeared in the *Journal* for April.

IV. LIBRARY.

The Report of the Joint Library Committee for 1940, and an extract from a report by the Chairman on the working of the Library during the past 20 years are given in Appendix B.

V. ADVISORY RESEARCH COUNCIL OF THE CHEMICAL SOCIETY.

The Advisory Research Council of the Chemical Society has continued to receive offers of assistance from Supervisors of Research, and has now allocated 173 topics of research to Research Workers. It has been unable to suggest topics to all those who have offered their services, and would welcome further suggestions, particularly those of a physico-chemical nature.

During the year a Scheme has been formulated in order to meet through the agency of volunteer workers demands for fine chemicals required for work of national importance and not available through the normal channels.

VI. ADMINISTRATION.

Local Representatives.

The resignations of Dr. J. A. V. Butler and Dr. A. B. Crawford from the office of Local Representatives for Edinburgh and Glasgow, respectively, were received with much regret, and the Council have appointed Dr. G. H. Christie and Dr. T. S. Stevens to fill the vacancies. Dr. E. A. Moelwyn-Hughes, who has deputised for Dr. F. B. Kipping as Local Representative for Cambridge, has had to relinquish office owing to temporary absence from Cambridge; Dr. F. S. Dainton has consented to act in his place.

VII. FINANCE.

(1) *Contributions.*

The Council have received contributions of £1150 from the Chemical Council and £550 from the Government Publications Grant (through the Royal Society) towards the cost of the Society's publications for 1940, and have expressed their sincere thanks for these substantial grants. The Council also acknowledged with gratitude the contributions received from the following Fellows to the Publications Fund: Messrs. P. Appleyard, R. H. Atkinson, P. K. Dutt, J. A. Newton Friend, W. E. Garner, F. W. Kirkbride, D. H. Peacock, W. G. Polack, J. E. B. Price, Sir David Rivett, R. Robison, H. G. Rule, F. C. Smith, R. B. Turbutt, and G. W. Young.

Valuable gifts of the Society's publications have been received from the following, to whom the thanks of the Council have been conveyed: Messrs. G. Adams, A. Bracher, H. E. Brothers, C. Fuller, P. J. Garner, J. W. Peck, L. M. Nash, H. E. Stevenson, G. A. Stokes, P. Szego, N. Garrod Thomas, Miss K. A. Cumming, Mrs. O. Gatty, and Imperial Chemical Industries, Ltd.

(2) *Bequests.*

The Council have received with gratitude a bequest of £100 under the Will of the late Mr. Emile Mond, which has been placed to the Special Reserve Fund; they are also pleased to announce that under the Will of the late Sir Gilbert Morgan, the income from the residuary estate, subject to life interests, has been left to the Society on certain conditions.

The following form of bequest has been approved by the Council:

> "I, ..., of ....., give and bequeath to The Chemical Society, Burlington House, Piccadilly, London, W. 1, free from deduction on account of any and every kind of death duty the sum of ..... for the use of The Chemical Society in such manner as the Council may in its absolute discretion determine. The receipt of the Treasurer or other Officer for the time being of The Chemical Society shall be a sufficient discharge for the same."

VIII. RELATIONS WITH OTHER BODIES.

(1) *The Chemical Council.*

The representatives of the Society on the Chemical Council were Professor F. G. Donnan, Mr. F. P. Dunn, and Professor I. M. Heilbron.

(2) *Representatives of the Society on other Bodies.*

During 1940, the Society was represented as follows :—

Bristol University Court :
Professor F. G. Donnan.
British National Committee for Chemistry :
Professor F. G. Donnan, Mr. F. P. Dunn (Treasurer), Dr. C. W. Davies (Senior Secretary).
British Standards Institution :
Council of Chemical Division : Dr. J. J. Fox.
Technical Committees :
Co-ordinating the work of the Divisional Councils in regard to any British Standard which may be issued in future for units, conversion factors, fundamental formulæ, values for properties of materials, etc. : Dr. H. J. T. Ellingham.
Specifications for Materials and Plant used in Electroplating : Dr. U. R. Evans.
Standardisation of Scientific Glassware : Mr. F. R. Ennos, Dr. E. B. Hughes.
Standards for use in Dairying Chemistry : Mr. Eric Voelcker.
Standardisation of Letter Symbols : Dr. C. F. Goodeve.
Bureau of Chemical and Physiological Abstracts :
Professor C. R. Harington, Dr. G. A. R. Kon, Dr. H. J. T. Ellingham, and one of the Hon. Secretaries, with the Treasurer, *ex-officio.*
City and Guilds of London Institute :
The President.
Faraday Society :
Colloid Committee : Mr. D. C. Henry.
Home Office :
Air-Raid Precautions Department : Mr. J. Davidson Pratt.
Joint Library Committee :
Professor A. J. Allmand, Professor H. Bassett, Dr. O. L. Brady, Professor C. H. Desch, Mr. M. B. Donald, Dr. H. J. Emeléus, Dr. C. F. Goodeve, Dr. P. Haas, Professor C. R. Harington, Dr. T. A. Henry, Dr. E. W. McClelland, Dr. E. E. Turner, Professor W Wardlaw, Dr. J. C. Withers.
Lawes Agricultural Trust :
Committee of Management : Dr. E. F. Armstrong.
Royal Microscopical Society :
Standardisation of Biological Stains : Professor A. G. Green.
Royal Society :
Joint Standing Committee for Symbols and Abbreviations : Dr. C. W. Davies, Dr. H. J. T. Ellingham.

IX. ACKNOWLEDGEMENTS.

The Council gratefully avail themselves of this opportunity of expressing their sincere thanks to the many Fellows who, notwithstanding prevailing conditions, have continued to give their services freely to the Society during the year. They would especially mention Local Representatives, those serving on Committees, refereeing papers for the *Journal*, contributing to the *Annual Reports*, and delivering lectures.

APPENDIX A.

REPORT OF THE BUREAU OF CHEMICAL AND PHYSIOLOGICAL ABSTRACTS FOR THE YEAR 1940.

The outstanding events of an exceptionally active year in the history of the Bureau have been the appointment of a new Chairman ; the appointment of an Honorary Treasurer, and the presentation to the Bureau of quarterly statements showing the financial position of the various sections of the Abstracts ; the decision of the participating Societies to extend the agreement for the production of Abstracts A III ; the decision of the Society of Chemical Industry to issue Abstracts B separately from the Transactions and in three parts, and the bringing of the Indexing staff completely under the control of the Bureau.

Eleven meetings of the Bureau were held during the year, as well as six meetings of the Finance Committee, and two of the A III Abstracts Sub-Committee.

The Chairman.—The Bureau suffered a great loss through the death, in February, of Sir Gilbert Morgan, who had filled the office of Chairman since 1933. Most fortunately the Bureau was able to persuade Dr. L. H. Lampitt to accept the Chairmanship.

Staff.—After twelve years' efficient service, Dr. J. J. Fox resigned his position as Assistant Editor in June. The Bureau has been fortunate in securing Dr. W. Jevons to fill the vacancy.

Finance.—With the cordial approval of the Societies, the Bureau, in March, appointed Mr. F. P. Dunn as its first Honorary Treasurer. The Finance Committee has been strengthened by the election of Professor C. R. Harington as an additional member. During the year the Finance Committee has been able, for the first time, to put before the Bureau quarterly statements showing the total costs of all sections of the monthly Abstracts, and of the Indexing Dept. The statements mentioned above show that the total cost of the Abstracts for 1940, including overhead expenses was as follows: A I and A II, £4767 2*s.* 7*d.*; A III, £4428; B, £5321 18*s.* 3*d.* Of these amounts the costs of the Indexing Dept. (including those of producing the 1939 Indexes, but excluding those due to the Quinquennial Index) were: A I and A II, £781 10*s.* 5*d.*; A III, £796 4*s.* 5*d.*; B, £991 17*s.* 2*d.*

Abstracts A III.—The agreement relating to the production of this section of the Abstracts terminated at the end of 1940, but as, in the opinion of the Societies concerned, this section of the Abstracts constitutes a valuable service to physiologists and biochemists, they decided unanimously to renew the agreement for a further three years. Despite an additional special grant of £200 from the Chemical Society and a grant of £50 from the Society of Chemical Industry, the production of these Abstracts showed a deficit of about £190 for the year, making a cumulative deficit of £388 for the three years' working. In order to meet this deficit and to ensure that this section of the Abstracts is maintained at its present standard, the Chemical Society agreed to increase its grant from £1300 to £1500 per annum, thus merging in the total grant the special contributions of £200 made in 1939 and 1940. The Physiological Society and the Biochemical Society each agreed to increase their grant by £100. It is hoped that, with the aid of this additional income and the increased subscription to the general public, it will be possible despite the probability of a reduction in the number of subscribers, to keep the expenditure within the income available and to eliminate the cumulative deficit during the next three years. The Bureau has recommended to the Chemical Society (which has since agreed to the recommendation) that in future the Accounts of Section A III of the Abstracts be issued as part of the Report of the Bureau and not as an appendix to the Report of the Council of the Chemical Society. The Accounts are appended hereto.

Abstracts Statistics.—The total number of abstracts published in 1940 was 28,779, as compared with 38,821 in 1939, a decrease of 10,023 (26%). The appended Table shows the number of abstracts and pages printed in each quarter of 1939 and 1940.

	A I.				A II.			
	1939.		1940.		1939.		1940.	
	No. of Abs.	Pages.	No. of Abs.	Pages.	No. of Abs.	Pages.	No. of Abs.	Pages.
1st quarter	1882	164	1471	136	713	134	606	112
2nd ,, ...	2119	182	1525	138	875	160	734	130
3rd ,, ...	1688	154	1200	106	906	170	444	78
4th ,, ...	1430	128	747	68	574	102	335	66
	7119	628	4943	448	3068	566	2119	386

	A III.				B.			
	1939.		1940.		1939.		1940.	
	No. of Abs.	Pages.	No. of Abs.	Pages.	No. of Abs.	Pages.	No. of Abs.	Pages.
1st quarter	4394	344	3225	276	3803	334	2798	250
2nd ,, ...	3818	296	3442	274	3656	340	2719	252
3rd ,, ...	3157	246	2858	230	3628	332	2380	208
4th ,, ...	2959	228	2169	166	3219	298	2126	194
	14,328	1114	11,694	946	14,306	1304	10,023	904

Of the 10,223 B abstracts 5540 were from journal literature and 4583 were abstracts of Patents (8509 and 5797 respectively in 1939).

The large decrease in the numbers of abstracts in all sections is due to the non-receipt, since June, of any publications from the enemy-occupied parts of Europe. The greater part of the European journals (including those from Germany) were received up to June, but the Bureau was unable to secure these in all cases. Much of the deficiency has been made up from journals abstracted at the Patent Office Library or loaned by the Science Library.

Annual Indexes.—The decision reached in December, 1939, to publish separate indexes of the 1939 Abstracts A and B has resulted in substantial savings both in paper and in money. 255 reams less paper were used (245 against 482) and the cost was £849 less (£1803 against £2652). Whilst a small part of the saving was due to the decreased size of the abstracts, the greater part is attributed to the division of the Index into two parts.

Improvement of Abstracts.—During the year the Bureau made an exhaustive series of enquiries among the staffs of large organisations (who frequently use Abstracts B) with the object of eliciting criticisms and suggestions for improvement. A summary of the results indicated that there was a general opinion in favour of a smaller type and the numbering of columns instead of pages to facilitate reference. These suggestions were adopted by the Bureau, and as it seemed desirable to keep the format of Abstracts A and B uniform, the recommendation was referred to the various Societies supporting the work of the Bureau. All the Societies agreed to the proposed changes. The cost of setting this smaller type per 1000 ems will be the same as at present, but a saving of about 27% is expected on machining, binding, and paper. Abstractors' fees will remain the same per number of words, but the rate will be raised from 10*s.* to 13*s.* 9*d.* per column. It is intended to apply the money saved to the improvement of the Abstracts. More notice will be given in Section A I to new principles and ideas in abstracts of theoretical and mathematical papers.

The report mentioned above also recommended *inter alia* that some of the abstracts should be more informative, while certain sections needed to be more comprehensive and the abstracts of Patent literature should be extended. These proposals were adopted by the Bureau for recommendation to the Council of the Society of Chemical Industry, who agreed with all these suggestions. As regards the extension of the abstracting of Patents, it is realised that at present this can apply only to those of the Dominions and Colonies. The Council of the Society of Chemical Industry has been asked for specific suggestions for enlarging the scope of journals covering *Abstracts B*.

The report also suggested that the sub-headings of the Subject Indexes should be more strictly alphabetical in arrangement. The Indexer has been instructed to carry this out.

Sub-division of B Abstracts.—The Society of Chemical Industry has adopted the recommendation of the Bureau to publish *Abstracts B* separately from the *Transactions* and in three sections: B I, General and Inorganic Industrial Chemistry; B II, Organic Industrial Chemistry; B III, Agriculture, Foods, Sanitation, etc. This change will take effect at the beginning of 1941.

Indexing Staff.—The staff of the Indexing Department has hitherto been under the control, partly of the Bureau and partly of the Chemical Society, each body having made the appropriate payments directly to the staff for work done. With the approval of the Chemical Society, the Indexing staff has now been placed entirely under the control of the Bureau, which makes all payments directly to the staff, and is reimbursed by the Chemical Society for work done by the staff on their behalf. The same procedure will be followed in respect of the indexing work carried on for other bodies.

Quinquennial Index.—Despite the difficulties imposed by war conditions work on the *Quinquennial Index* 1933—1937 has proceeded steadily during the year, and the Bureau is glad to announce that the first volume (Authors Names, 1964 pages) was completed at the end of the year. It is expected that the Subject Index will be published before the end of 1941. Sufficient paper for the whole work has been secured.

BUREAU OF CHEMICAL AND PHYSIOLOGICAL ABSTRACTS.

INCOME AND EXPENDITURE ACCOUNT OF ABSTRACTS A III FOR THE YEAR ENDED 31ST DECEMBER, 1940.

1939 £ s. d.	1939 £ s. d.	*Income.*	1940 £ s. d.	1940 £ s. d.
	2350 9 5	To Sales of Abstracts A III		2050 8 5
	2 10	„ Sales of Physiological Abstracts (proportion)		10 6
		„ Contributions :		
1300 0 0		The Chemical Society (Annual Grant) ...	1300 0 0	
200 0 0		„ „ „ (Additional Grant) ...	200 0 0	
300 0 0		The Physiological Society (Annual Grant) ...	300 0 0	
200 0 0		The Biochemical Society „ „ ...	200 0 0	
100 0 0		The Anatomical Society „ „ ...	100 0 0	
—		The Society of Chemical Industry (Special Grant)	50 0 0	
	2100 0 0			2150 0 0
	3 10 6	„ Interest on Deposit		2 5 6
49 13 5		„ Proceeds of Advertisements	49 10 9	
14 0 0		*Less* Commission	14 0 0	
	35 13 5			35 10 9
	307 2 10	„ Excess of Expenditure over Income, carried to Balance Sheet		189 12 9
	£4796 19 0			£4428 7 11

1939 £ s. d.	1939 £ s. d.	*Expenditure.*	1940 £ s. d.	1940 £ s. d.
494 17 10		By Editorial Salaries	510 5 9	
46 0 5		„ „ Postages	25 9 5	
1798 0 2		„ Printing and Paper	1607 4 2	
31 10 10		„ Banding	30 1 6	
239 2 10		„ Distribution	181 13 1	
1088 4 5		„ Abstractors' Fees	927 8 10	
61 6 8		„ Miscellaneous	100 9 1	
		„ Index :	£ s. d.	
147 9 3		Editorial Salaries	235 16 3	
10 2 2		Superannuation	11 2 7	
622 18 2		Printing and Paper	482 1 2	
13 9 9		Banding	10 19 7	
51 13 11		Distribution	34 16 1	
42 2 7		Miscellaneous	33 15 7	
				808 11 3
150 0 0		„ Overhead Expenses (Proportion Chemical Society		160 4 5
—		„ Overhead Expenses (Proportion) Society of Chemical Industry		77 0 5
	4796 19 0			4428 7 11
	£4796 19 0			£4428 7 11

BALANCE SHEET OF ABSTRACTS A III FOR THE YEAR ENDED 31ST DECEMBER, 1940.

Liabilities.	£ s. d.	£ s. d.	*Assets.*	£ s. d.	£ s. d.
To Sundry Creditors	1249 7 0	946 6 7	By Sundry Debtors		393 12 4
			„ Cash at Bank		355 17 7
			„ Excess of Expenditure over Income for year	189 12 9	
			Less Excess of Income over Expenditure brought forward	—	
			Add Excess of Expenditure over Income brought forward	198 16 8	
					388 9 5
	£1249 7 0	£946 6 7			£1249 7 0

The appended statement shows the position of the Quinquennial Index Fund at the end of 1940.

Offices.—The work of the Bureau was temporarily disorganised by enemy action, which caused the removal of the offices from Clifton House to South Kensington. Fortunately, however, only a small quantity of the property of the Bureau was lost, and it has proved possible to publish the Abstracts with the usual regularity. As some of the Editorial Staff has moved from London, additional time is consumed by postal communications, and some delay occurred in the production of the individual abstracts.

QUINQUENNIAL INDEX ACCOUNT.

1938.

	£	s.	d.		£	s.	d.
Subscriptions (*less* refunds and loss on Exchange £148 12*s.* 8*d.*)	1253	13	4	Repayment of loan from Decennial Index Account	25	0	0
				Salaries	198	10	4
				Rent	33	15	0
				Sundry Expenses	82	19	4
				Insurance	1	15	0
					341	19	8
				Balance	911	13	8
	£1253	13	4		£1253	13	4

1939.

	£	s.	d.		£	s.	d
Balance forward	911	13	8	Salaries	381	8	1
Subscriptions (less refunds £1)...	257	9	11	Rent	45	0	0
Grants:				Sundry Expenses	33	14	3
Royal Society	250	0	0	Insurance		12	6
Chemical Council	250	0	0				
Bank Interest		18	1		460	14	10
				Balance	1209	6	10
	£1670	1	8		£1670	1	8

1940.

	£	s.	d.		£	s.	d.
Balance forward	1209	6	10	Salaries	350	14	4
Subscriptions (less refunds £7 14*s.* 0*d.*)	45	15	6	Rent	45	0	0
				Paper	264	17	8
Grant:				Sundry Expenses	32	9	11
Royal Society	250	0	0	Insurance	1	13	3
					694	15	2
				Balance	810	7	2
	£1505	2	4		£1505	2	4

APPENDIX B

ANNUAL REPORT OF THE JOINT LIBRARY COMMITTEE, 1940.

During the year there were 4381 attendances as compared with 7009 in 1939. Of these 2344 were made by Fellows of the Chemical Society, and 2037 by Members of other Constituent and Contributing Bodies, as against 3926 and 3083 in 1939.

The number of books borrowed was 4307, against 4861 in the previous year, of these 1702 were issued by post, compared with 1444 in the preceding year.

The Library telephone facilities are still made use of, and the incoming calls included 741 enquiries which necessitated reference to books in the Library, as against 962 the previous year.

The additions to the Library comprise:

115 books, of which 40 were presented, 432 volumes of periodicals and 202 pamphlets, as against 251 books, 723 volumes of periodicals and 242 pamphlets, last year.

Analysis.

	Attendances.	Books borrowed.	Books added.	Volumes of periodicals.	Pamphlets.
1940	4381	4307	115	432	202
1939	7009	4861	251	723	242

The total number of volumes added during the year was 547. The Library now contains 44,193 volumes, consisting of 13,167 books and 31,026 bound volumes of periodicals.

The Committee wishes to record its grateful appreciation of the gifts received from Fellows and others during the year.

The Committee desires to place on record its keen appreciation of the valuable service Dr. Brady has rendered during his tenure of office as Chairman of the Joint Library Committee and in particular of his long-continued work in furtherance of co-operative support of the Library by the Societies which serve the interests of chemists in this country.

EXTRACTS FROM A REPORT OF THE JOINT LIBRARY COMMITTEE ON LIBRARY CO-OPERATION DURING TWENTY YEARS.

The scheme of Library co-operation between the various chemical bodies was initiated in 1919, and has thus been in operation a little over twenty years. The time, therefore, seems opportune to review the position.

In 1919 the Council of the Chemical Society offered to allow Members of a number of other chemical bodies to make use of the Library of the Chemical Society in return for voluntary contributions towards the cost of running the Library to be made by the societies accepting the offer on behalf of their members. This proposal was accepted by the Institute of Chemistry, the Society of Chemical Industry, and other Societies. Representation on the Library Committee of the Chemical Society was given to the contributing bodies and as these were largely concerned with chemical practice the policy of the Library Committee as regards the purchase of books was modified with the object of making the Library fully representative of all branches of pure and applied chemistry. Although previously books on technical chemistry had been acquired, from 1919 onwards the purchase of such works has been greatly extended.

In 1935 the setting up of the Chemical Council by agreement between the Chemical Society, the Institute of Chemistry, and the Society of Chemical Industry afforded an opportunity of closer co-operation between these three bodies in support of a national chemical library.

In practice, therefore, the Library of the Chemical Society became, for the period of the agreement, a national chemical Library under the management of the three societies as represented by the Chemical Council and the Joint Library Committee. All expenditure on maintenance is considered by the Joint Library Committee and submitted to the Chemical Council for its approval.

The cost of purchase of books, periodicals, binding, and furniture is met solely by the Chemical Society. The Joint Library Committee makes recommendations on these matters to the Council of the Chemical Society which authorizes the expenditure.

It is noteworthy that, so far, the Council of the Chemical Society has never denied the funds necessary for the purchase of all books recommended by the Joint Library Committee. In addition, the Chemical Society exchanges sets of its publications with

sets of chemical publications of other bodies all over the world; these are ultimately presented to the Library, and represent a very considerable additional contribution from the Chemical Society.

Finance.

Since the agreement between the three main bodies the Association of British Chemical Manufacturers and a number of other scientific societies have continued to make voluntary contributions towards the maintenance of the Library in return for privileges for their members. Their contributions, together with a grant of £150 from the Chemical Society, amounted to £382; the balance of £1535 being, in accordance with the agreement, devised as follows: Institute of Chemistry £718, the Society of Chemical Industry £410, and the Chemical Society £407.

The expenditure on maintenance represents a sum of the order of 2*s.* per member of the various societies, and for this sum they enjoy full use of one of the finest chemical Libraries in the world.

The Chemical Society in this year expended £722 on purchase of books, periodicals (other than those received in exchange), and binding, representing an additional expenditure of about 4*s.* per member.

Use of the Library.

The use of the Library has more than doubled in the twenty years under review. Compared with 1919, for which year the figures are given in brackets, in 1938 there were 8507 (3898) attendances; of these 4803 (3299) were by members of the Chemical Society, but many of them were also members of the Institute of Chemistry and/or the Society of Chemical Industry; 3704 (599) were by non-members of the Chemical Society, made up of 2709 (229) by members of the Institute of Chemistry, 704 (288) by members of the Society of Chemical Industry, and 291 (82) by members of other contributing bodies.

The total books borrowed were 5948 (2867), of which 1697 (929) were sent by post; of these 3429 (2549) were borrowed by members of the Chemical Society and 2519 (318) by non-members of the Chemical Society, made up of 1930 (161) by members of the Institute of Chemistry, 426 (143) by members of the Society of Chemical Industry, and 163 (14) by members of other contributing bodies.

Contents of the Library.

At the beginning of 1919 there were in the Library 6564 books and 16,753 bound volumes of periodicals; at the end of 1938 there were 12,801 books and 29,871 bound volumes of periodicals. At present the number of additions of bound volumes per annum is over 950. The Library covers every aspect of chemistry and is exceptionally strong in periodicals (as defined by the World List of Scientific Periodicals), the titles under this heading being 1022. No less than 127 of the important ones are in duplicate, and consequently available to borrowers. A photostat service is available by means of which readers can obtain copies of papers, etc., for their own personal use at reasonable cost.

It might be of interest to users of the Library if the procedure by which the Library is kept up to date is outlined. At every meeting of the Joint Library Committee a list of all the new books on pure and applied chemistry and related topics, British and foreign, published since the last meeting, is submitted by the Librarian, many of them are on the table for inspection. Previously some expert has been written to and asked to express an opinion on the value of the book. Each book is then considered individually and its purchase recommended or not. Sometimes the purchase of a book is postponed to discover if it is asked for by some reader. It is not the policy of the Committee to purchase every book and every new edition. Among the considerations which weigh with new books are, not necessarily in this order, (*a*) the report of the expert, (*b*) the distinction of the author, (*c*) the strength of the Library in this section, (*d*) the demand of readers for this particular type of book; with new editions the popularity of the previous edition and the amount of change are usually considered. The Librarian, from his reference cards, is able to supply the Committee with such information as it requires on these matters.

The Future.

The outbreak of war has made it impossible to foretell future developments. For some time now there has been no room for expansion of the Library at Burlington House. Room was found last year for the regular additions by storage of certain little-used journals available elsewhere in Burlington House, and the removal of certain valuable books to safer quarters as a war precaution has provided some temporary space. From now on, however, the efficiency of the Library must suffer until more accommodation is available. This matter has been engaging the serious attention of the Joint Library Committee and the Council of the Chemical Society for some time, and a number of alternative plans were under consideration; the crisis of September 1938 made progress difficult, and the present emergency has necessitated their temporary abandonment. The policy of the Joint Library Committee is to provide for British chemists the best possible Library facilities that present circumstances allow, and when better times arrive to press forward with their schemes for adequate accommodation.

APPENDIX C

LECTURES AND DISCUSSIONS.

Lectures given in London.

18th January, on "New Views on Colloid Chemistry," by Professor J. D. Bernal; 15th February, "Urbain Memorial Lecture," by Dr. A. S. Russell; 4th April, "Sörensen Memorial Lecture," by Professor E. K. Rideal.

Lectures given outside London.

Birmingham. At the University, Edgbaston: 19th February, *Tilden Lecture* on "Recent Progress in the Chemistry of Plant Gums and Pectic Materials," by Professor E. L. Hirst; 22nd October, lecture on "The Constituents of Natural Phenolic Resins," by Professor R. D. Haworth.

Bristol. At the University (Joint Meeting with the Local Sections of the Institute of Chemistry and the Society of Chemical Industry): 29th February, lecture on "The Mechanism of the Synthesis of Large Molecules," by Dr. H. W. Melville; 3rd October, lecture on "By-Products of Industrial Research," by Dr. Gwyn Williams.

Edinburgh. At the North British Station Hotel (Joint Meeting with the Local Sections of the Institute of Chemistry and the Society of Chemical Industry): 22nd January, lecture on "Proteins under the X-Rays," by Dr. W. T. Astbury; at Heriot-Watt College (Joint Meeting with the Edinburgh University Chemical Society, the Institute of Chemistry, and the Society of Chemical Industry), 26th November, lecture on "The Chemical Exploration of the Stratosphere," by Professor F. A. Paneth.

Glasgow. Royal Technical College (Joint Meeting with the Local Sections of the Institute of Chemistry and the Society of Chemical Industry, the Alchemists Society and the Andersonian Chemical Society): 16th February, lecture on "Ionisation and its Chemical Significance," by Professor W. F. K. Wynne-Jones; at the University, 14th October, lecture on "Synthetic Oestrogens," by Professor E. C. Dodds; at the Royal Technical College, 15th November, lecture on "The Structure of Proteins," by Dr. W. T. Astbury.

Leeds. At the University: 14th October, lecture on "The Constituents of the Natural Phenolic Resins," by Professor R. D. Haworth.

Liverpool. At the University (Joint Meeting with the Liverpool University Chemical Society): 31st October, lecture on "Recent Work on the Chemistry of Protozoal Infections," by Professor Warrington Yorke.

Manchester. At the University (Joint Meeting with the Manchester Section of the Society of Chemical Industry and other Societies): 9th November, lecture on "Coal Rank and Structure," by Professor H. L. Riley.

North Wales. At University College, Bangor (Joint Meetings with the University College of North Wales Chemical Society): 23rd February, lecture on "William Hyde Wollaston," by Mr. L. F. Gilbert; 8th March, lecture on "The Chemist in the Garden," by Mr. H. J. Evans.

Nottingham. At University College: 2nd February, lecture on "Application of Reaction Kinetics to Problems of Organic Chemistry," by Dr. H. B. Watson; at the Welbeck Hotel (Joint Meeting with the Local Section of the Institute of Chemistry and the Society of Chemical Industry), 7th March, lecture on "Hormones," by Professor E. C. Dodds; (Joint Meeting with the Local Section of the Institute of Chemistry), 14th November, lecture on "Stereochemistry and Valency Group," by Professor N. V. Sidgwick: at University College (Joint Meeting with the University College Physical and Chemical Society), 28th November, lecture on "Bivalent Hydrogen; Some New Aspects of Tautomerism," by Dr. L. Hunter.

St. Andrews and Dundee. At University College, Dundee: 25th November, lecture on "The Chemical Exploration of the Stratosphere," by Professor F. A. Paneth.

Sheffield. At the University: 19th February, *Tilden Lecture* on "The Present State of Valency Theory," by Dr. L. E. Sutton; 8th March, lecture on "Biological Applications of Synthetic Chemistry," by Professor J. W. Cook; (Joint Meeting with the Sheffield University Chemical Society), 8th November, lecture on "Reactions in Monolayers," by Professor E. K. Rideal.

South Wales.

Cardiff. At University College (Joint Meeting with the Chemical and Physical Society of University College of South Wales): 16th February, lecture on "Recent Work in the Investigation of Molecular Structure," by Dr. F. G. Mann; (Joint Meeting with the Local Sections of the Institute of Chemistry and the Society of Chemical Industry), 18th October, lecture on "Some Recent Developments in Microchemistry," by Dr. Janet W. Matthews; (Joint Meeting with the Local Sections of the Institute of Chemistry and the Society of Chemical Industry), 7th December, lecture on "Some New Developments in the Petroleum Industry," by Mr. W. W. Williams.

Swansea. At the Royal Institution of South Wales (Joint Meeting with the University College of Swansea Chemical Society): 9th November, lecture on "Fluorine: Some Recent Developments in the Chemistry of the Element and its Derivatives," by Dr. H. J. Emeléus; (Joint Meeting with the University College of Swansea Chemical Society and the Local Section of the Institute of Chemistry), 23rd November, lecture on "Some Aspects of Surface Action," by Professor E. K. Rideal.

INCOME AND EXPENDITURE GENERAL PURPOSES ACCOUNT FOR THE YEAR ENDED 31ST DECEMBER, 1940.

1939 £ s. d.	1939 £ s. d.	*Income.*	1940 £ s. d.	1940 £ s. d.
	23 10 0	To Life Composition Fees (£180 0*s.* 0*d.*), one-third as Income		60 0 0
		„ Annual Subscriptions :		
997 8 10		Received in advance, on account of 1940 ...	668 16 8	
7545 9 11		„ during 1940 „ „ „ ...	7522 4 11	
292 15 4		„ „ „ „ „ 1939 ...	308 12 8	
23 7 6		„ „ „ „ „ 1938 and previous years	3 12 2	
8859 1 7			8503 6 5	
320 0 0		*Less* Amount included in last year's Income, being valuation of Arrears as per last Balance Sheet	270 0 0	
8539 1 7			8233 6 5	
270 0 0		*Add* Arrears at date : £797 18*s.* 6*d.* Estimated to realise as per Balance Sheet ...	270 0 0	
	8809 1 7			8503 6 5
	780 8 10	„ Dividends on Investments		625 18 5
	279 9 5	„ Income Tax recovered		351 3 9
	5 12 4	„ Interest on Deposit		3 11 2
	—	„ Donations		5 0 0
	39 0 1	„ Miscellaneous Receipts		45 11 6
	321 9 9	„ Excess of Expenditure over Income carried to Balance Sheet		463 10 11
	£10,258 12 0			£10,058 2 2

1939 £ s. d.	1939 £ s. d.	*Expenditure.*	1940 £ s. d.	1940 £ s. d.
		By Administration Expenses :		
2389 14 5		Office Salaries and Wages	2415 8 2	
255 18 6		Superannuation	259 13 0	
313 17 10		House Expenses, etc.	314 8 11	
84 0 0		Accountants' Charges	84 0 0	
323 1 10		Miscellaneous Printing and Stationery ...	291 1 0	
186 11 11		Postages	191 17 6	
77 7 2		Miscellaneous	53 11 4	
3630 11 8			3609 19 11	
		Less Transfer to Publications and Library : £ *s.* *d.*		
320 0 0		Journal 333 3 0		
170 0 0		Abstracts A I, A II 276 17 3		
150 0 0		„ A III 160 4 5		
199 15 1		Library Account 163 19 11		
	2790 16 7		934 4 7	2675 15 4
	212 18 5	„ Expenses of Meetings		35 19 5
	5 5 0	„ Donations		5 5 0
	5618 10 5	„ Contribution to Publications Fund		6055 8 6
		„ Contribution to Library Fund :		
605 7 0		For Fittings, Furniture, Books, Periodicals, and Binding	340 15 1	
136 15 7		For Aid Raid Precautions	68 3 8	
346 16 1		Proportion of Maintenance	327 11 11	
1088 18 8			736 10 8	
88 12 1		*Less* Balance from Library Account	16 7 7	
	1000 6 7			720 3 1
	38 18 0	„ Transfer to Staff Pensions Fund		38 17 10
	200 0 0	„ Transfer to Centenary Fund		200 0 0
	87 10 11	„ Expenses of Local Representatives		66 16 0
	—	„ Legal Expenses		3 3 0
	5 17 6	„ Interest on Loans from other Funds		4 18 8
	298 8 7	„ Air Raid Precautions		251 15 4
	£10,258 12 0			£10,058 2 2

Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1940.

PUBLICATIONS FUND.

1939 £ s. d.	1939 £ s. d.	*Income.*	1940 £ s. d.	1940 £ s. d.
		To Publication Sales (including back numbers):		
3250 16 5		Journals and Proceedings	2768 6 2	
2069 10 5		Abstracts, A I, A II	1894 8 9	
6 5 4		Collective Index, Vols. I–VI	10 13	
20 0 0		„ „ 1923–32	—	
1032 6 8		Annual Reports on Progress of Chemistry ...	871 14 10	
286 12 8		Authors' Extra Reprints	253 13 0	
3 18 5		Other Publications	5 15 6	
	6669 9 11			5804 11 6
		„ Proceeds of Advertisements:	£ s. d.	
502 2 5		Journal	442 16 1	
80 19 6		Annual Reports	58 9 6	
583 1 11			501 5 7	
171 0 8		*Less* Commission	143 15 2	
	412 1 3			357 10 5
49 13 5		A I, A II	49 10 9	
14 0 0		*Less* Commission	14 0 0	
	35 13 5			35 10 9
				393 1 2
		„ Donations:		
12 12 6		Fellows	11 3 0	
1000 0 0		Chemical Council	1000 0 0	
150 0 0		„ for Summaries to Papers in "Journal"	150 0 0	
	1162 12 6			1161 3 0
	600 0 0	„ Government Publications Grant (through the Royal Society)		550 0 0
	289 16 10	„ Dividends on Investments		247 0 6
	118 17 6	„ Income Tax recovered		145 15 8
	5618 10 5	„ Transfer from General Purposes Account (the balance of expenditure on publications) ...		6055 8 6
	£14,907 1 10			£14,357 0 4

1939 £ s. d.	1939 £ s. d.	*Expenditure.*	1940 £ s. d.	1940 £ s. d.
		By Expenses on account of Journal:		
1160 3 9		Editorial Salaries	1159 11 9	
85 12 6		Superannuation	85 12 6	
33 10 8		Editorial Postages	24 5 7	
3673 6 6		Printing and Paper	3098 14 2	
53 13 11		Banding	54 5 8	
669 11 5		Distribution	552 12 0	
639 7 4		Authors' Reprints	516 15 6	
16 6 11		Miscellaneous	14 3 2	
320 0 0		Overhead Expenses (proportion)	333 3 0	
	6651 13 0			5839 3 4
		„ Expenses on account of Abstracts A I, A II:		
667 4 11		Editorial Salaries	732 9 2	
44 16 2		Editorial Postages	29 7 1	
1163 13 8		Abstractors' Fees	817 8 11	
2196 0 8		Printing and Paper	1674 15 6	
51 5 2		Banding	52 0 0	
262 3 5		Distribution	225 14 6	
66 13 7		Miscellaneous	98 5 10	
		„ Index:	£ s. d.	
157 14 3		Editorial Salaries	208 7 0	
10 16 8		Superannuation	9 16 3	
614 1 5		Printing and Paper	490 1 8	
11 0 9		Banding	13 11 8	
51 11 2		Distribution	43 1 3	
45 13 6		Miscellaneous	29 17 0	
				794 14 10
170 0 0		Overhead Expenses (proportion) Chemical Society		276 17 3
141 6 9		Overhead Expenses (proportion) Society Chemical Industry		65 9 6
	5654 2 1			4767 2 7
1300 0 0		„ Agreed contribution to Abstracts A III ...	1300 0 0	
200 0 0		„ Additional contribution to Abstracts A III ...	200 0 0	
	1500 0 0			1500 0 0
		„ Transfer to Special Reserve Fund for publications		1100 0 0
	300 0 0	„ Reserve for Quinquennial Index, 1933–1937		300 0 0
		„ Annual Reports on the Progress of Chemistry:		
	801 6 9	Printing and Honoraria		850 14 5
	£14,907 1 10			£14,357 0 4

Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1940.

LIBRARY.

1939						*Income.*	1940					
£	s.	d.	£	s.	d.		£	s.	d.	£	s.	d.
						To Contribution for Fittings, Furniture, Books, Periodicals and Binding:						
605	7	0				Transfer from General Purposes Account ...	340	15	1			
200	0	0				„ „ Herbert Spencer Bequest ...	200	0	0			
			805	7	0					540	15	1
						„ Air Raid Precautions:						
			136	15	7	Transfer from General Purposes Account ...				68	3	8
						„ Contributions through the Chemical Council towards maintenance:						
						Chemical Society (transfer from General Purposes Account)	327	11	11			
346	16	1										
715	5	9				Institute of Chemistry	682	11	4			
382	18	8				Society of Chemical Industry	354	19	5			
250	0	0				The Chemical Council	250	0	0			
			1695	0	6					1615	2	8
						„ Contributions, etc., received from other sources towards maintenance:						
						Association of British Chemical Manufacturers						
100	0	0					100	0	0			
21	0	0				Biochemical Society	21	0	0			
26	5	0				Faraday Society	26	5	0			
50	0	0				Institute of Brewing	50	0	0			
10	10	0				Society of Dyers and Colourists	10	10	0			
21	0	0				Society of Public Analysts	21	0	0			
3	0	0				Fellows	3	0	0			
5	14	3				Miscellaneous receipts	5	19	4			
			237	9	3					237	14	4
			£2874	12	4					£2461	15	9

1939						*Expenditure.*	1940					
£	s.	d.	£	s.	d.		£	s.	d.	£	s.	d.
						By Capital Expenditure:						
573	10	0				Books and Periodicals *	208	6	1			
						Transfer to Special Reserve Fund for Books and Binding...	200	0	0			
80	0	0										
151	17	0				Binding	132	9	0			
136	15	7				Air Raid Precautions	68	3	8			
			942	2	7					608	18	9
						„ Maintenance:						
1443	10	0				Salaries	1465	19	6			
177	15	6				Superannuation of Library Staff	181	1	0			
14	15	8				Postages	17	12	10			
8	1	5				Miscellaneous Expenses	7	16	2			
199	15	1				Overhead Expenses (proportion)	163	19	11			
			1843	17	8					1836	9	5
			88	12	1	„ Balance transferred to General Purposes Account				16	7	7
			£2874	12	4					£2461	15	9

* Other than those received in exchange.

Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1940.

RESEARCH FUND.

1939			*Income.*	1940			1939			*Expenditure.*	1940		
£	s.	d.		£	s.	d.	£	s.	d.		£	s.	d.
448	5	9	To Dividends on Investments	438	2	7	20	0	0	By Honorarium, Longstaff Medallist	—	—	—
163	13	4	„ Income Tax recovered	224	4	11	2	0	0	„ Longstaff Medal	—	—	—
94	3	9	„ Repayment of Grants	67	9	8	404	0	0	„ Grants	210	10	0
10	0	0	„ Grants not applied for	4	0	0	8	9	11	„ Miscellaneous Expenses	5	10	0
12	4	6	„ Interest on Deposit	5	11	10				„ Balance, being Excess of Income over Expenditure, carried to Balance Sheet	528	2	1
	3	9	„ Interest on Loan to General Purposes Account		3	11	294	1	2				
—	—	—	„ Sale of Apparatus	4	9	2							
£728	11	1		£744	2	1	£728	11	1		£744	2	1

SPECIAL PUBLICATIONS FUND.

Income.									*Expenditure.*				
£	s.	d.	£	s.	d.		£	s.	d.	£	s.	d.		£	s.	d.
			To Sales of Publications:													
3	17	0	Memorial Lecture, Vol. I.				6	15	3							
4	7	6	Do. Vol. II.				5	2	0							
5	3	8	Do. Vol. III.				7	19	9							
2	6	10	Faraday Lectures				3	2	6							
2	3	10	Portraits				1	8	10							
5	0	3	Other publications				1	1	9							
				22	19	1				25	10	1				
				74	0	8				74	0	8				
			„ Dividend on Investments	2	6	0				3	19	11				
			„ Interest on Deposit	1	9	4					11	5				
			„ Interest on Loan to General Purposes Account													
				£100	15	1				£104	2	1		£100	15	1

£	s.	d.	*Expenditure.*	£	s.	d.
13	3	8	By Reprints for Memorial Lectures, Vol. IV.	3	11	6
—	—	—	„ Reprints for Faraday Lectures, Vol. II.	8	11	1
87	11	5	„ Excess of Income over Expenditure carried to Balance Sheet	91	19	6
£104	2	1		£104	2	1

Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1940.

SPECIAL LECTURES FUND.

1939	*Income.*	1940	1939	*Expenditure.*	1940
£ s. d.		£ s. d.	£ s. d.		£ s. d.
39 2 5	To Dividends on Investments	35 13 0	25 0 0	By Honorarium	— — —
6 7 1	„ Income Tax recovered	8 1 10	9 2 0	„ Lecture Expenses	— — —
18 3	„ Interest on Deposit	17 0		„ Balance, being Excess of Income over Expenditure, carried to Balance Sheet	44 11 10
1 1	„ Interest on Loan to General Purposes Account	— — —	12 6 10		
£46 8 10		£44 11 10	£46 8 10		£44 11 10

STAFF PENSIONS FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
38 18 0	To Transfer from General Purposes Account	38 17 10	80 0 0	By Pension paid during 1940	80 0 0
35 19 10	„ Dividends on Investments	34 12 0			
5 2 2	„ Income Tax recovered	6 10 2			
£80 0 0		£80 0 0	£80 0 0		£80 0 0

THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
38 11 2	To Dividends on Investments	32 5 6	150 0 0	By Harrison Prize	— — —
13 16 0	„ Income Tax recovered	17 11 4	6 15 0	„ Harrison Plaque	— — —
14 5	„ Interest on Deposit	10 11		„ Balance, being Excess of Income over Expenditure, carried to Balance Sheet	50 7 9
103 13 5	„ Excess of Expenditure over Income, carried to Balance Sheet	— — —	— — —		
£156 15 0		£50 7 9	£156 15 0		£50 7 9

Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1940.

CENTENARY FUND.

1939	Income.	1940
£ s. d.		£ s. d.
5 5 0	To Donations	— — —
200 0 0	„ Contribution from General Purposes Account	200 0 0
14 19 7	„ Interest on Deposit in Post Office Savings Bank and London Savings Bank	19 7 7
3 2 6	„ Interest on Loan to General Purposes Account	3 19 2
£223 7 1		£223 6 9

1939	Expenditure.	1940
£ s. d.		£ s. d.
62 10 0	By Honorarium	223 6 9
160 17 1	„ Excess of Income over Expenditure carried to Balance Sheet	
		£223 6 9

THE HERBERT SPENCER BEQUEST.

£ s. d.	Income.	£ s. d.
4 14 1	To Interest on Deposit in Post Office Savings Bank and London Savings Bank	17 10
1 0 10	„ Interest on Loan to General Purposes Account	4 2
216 0 1	„ Excess of Expenditure over Income carried to Balance Sheet	232 18 0
£221 15 0		£234 0 0

£ s. d.	Expenditure.	£ s. d.
200 0 0	By Transfer to Library Account for purchase of Books	200 0 0
21 15 0	„ Purchase of Office Furniture	34 0 0
		£234 0 0

THE FARADAY LECTURE FUND.

£ s. d.	Income.	£ s. d.
9 10 4	To Dividends on Investments	7 11 0
1 16 1	„ Income Tax recovered	4 11 10
£11 6 5		£12 2 10

£ s. d.	Expenditure.	£ s. d.
11 6 5	By Excess of Income over Expenditure carried to Balance Sheet	12 2 10
		£12 2 10

THE TILDEN LECTURE FUND.

£ s. d.	Income.	£ s. d.
51 16 9	To Dividends on Investments	48 2 7
8 8 0	„ Income Tax recovered	20 6 9
5 2	„ Interest on Deposit	7 6
£60 9 11		£68 16 10

£ s. d.	Expenditure.	£ s. d.
15 15 0	By Honorarium	15 15 0
14 1	„ Lecture Expenses	2 19 2
	„ Transfer to General Purposes Account, for cost of publication of Lecture	12 12 0
44 0 10	„ Excess of Income over Expenditure carried to Balance Sheet	3. 10 8
£60 9 11		£68 16 10

THE CHEMICAL SOCIETY.—BALANCE SHEETS, 31st December, 1940.

GENERAL PURPOSES.

1939			*Liabilities.*	1940				1939			*Assets.*	1940		
£	s.	d.		£	s.	d.	£	s.	d.		£	s.	d.
			670 0 8				To Subscriptions received in advance ...						
			2,763 0 4				„ Sundry Creditors (Printing and other Expenses)						
			600 0 0				„ Reserve for Quinquennial Index, 1933–1937						
							„ Loans from other Funds:						
550	0	0					Special Publications Fund	600	0	0			
750	0	0					Centenary Fund						
250	0	0					Herbert Spencer Bequest						
400	0	0					Research Fund	700	0	0			
							Special Lectures Fund	100	0	0			
							„ Reserve Fund	500	0	0			
			1,950 0 0										
			2,500 0 0				„ Loan, The Chemical Council						
							„ Excess of Assets over Liabilities as per last Balance Sheet	21,888	19	10			
							Add Amount received from Executors of Emile Mond—Legacy	100	0	0			
							Add Life Composition Fees (two-thirds)	120	0	0			
							Add Profit on Surrender of £700 Canada 3½% Stock						
							Add Amount on deposit with United Kingdom Provident Institution *re* Superannuation	2,018	2	9			
								24,127	2	7			
							Deduct Excess of Expenditure over Income for year £ s. d. 463 10 11						
							Deduct Amount transferred to Special Reserve Fund: Emile Mond Legacy ... 100 0 0						
								563	10	11			
			21,888 19 10					23,563	11	8			
			£30,372 0 10					£31,409	14	5	£30,372 0 10	£31,409	14	5

SPECIAL RESERVE FUND.

£	s.	d.		£	s.	d.	£	s.	d.	£	s.	d.		£	s.	d.
			To Cash transferred:										By Investments as per Schedule (cost or value when acquired)	800	0	0
—			Emile Mond Bequest	100	0	0				—			„ Loan to General Purposes Account	500	0	0
—			Reserve for Library Books (Balance 1939 transferred) ...	50	16	0				—			„ Sundry Debtor	100	0	0
—			Reserve for Library Books and Binding	200	0	0				—			„ Cash at Bank	50	16	0
—			Reserve for Publications	1100	0	0										
							1450	16	0							
							£1450	16	0					£1450	16	0

The Chemical Society. Balance Sheets, 31st December, 1940.

PUBLICATIONS FUND.

1939	*Liabilities.*		1940	1939	*Assets.*	1940
£ s. d.		£ s. d.	£ s. d.	£ s. d.		£ s. d.
9363 3 10	To Excess of Assets over Liabilities as per last Balance Sheet	9363 3 10	9363 3 10	9363 3 10	By Investment as per Schedule (cost or value when acquired)	9363 3 10

RESEARCH FUND.

£ s. d.	£ s. d.	*Liabilities.*	£ s. d.	£ s. d.	£ s. d.	*Assets.*	£ s. d.
	350 0 0	To Sundry Creditors		49 14 2	16,675 18 0	By Investments as per Schedule (cost or value when acquired)	18,275 18 0
		„ Excess of Assets over Liabilities as per			— — —	„ Sundry Debtors	3 11
14,749 19 10		last Balance Sheet	17,044 1 0		400 0 0	„ Loan to General Purposes Account	700 0 0
2,000 0 0		*Add* Amount received from Trustees of W. S. Gilles—Legacy	1,600 0 0		318 3 0	„ Cash at Bank	245 15 4
16,749 19 10			18,644 1 0				
294 1 2		*Add* Excess of Income over Expenditure for year	528 2 1				
	17,044 1 0			19,172 3 1			
	£17,394 1 0			£19,221 17 3	£17,394 1 0		£19,221 17 3

SPECIAL PUBLICATIONS FUND.

£ s. d.	£ s. d.	*Liabilities.*	£ s. d.	£ s. d.	£ s. d.	*Assets.*	£ s. d.
	13 3 8	To Sundry Creditors		— — —	1600 0 0	By Investment as per Schedule (cost or value when acquired)	1600 0 0
		„ Excess of Assets over Liabilities as per last			— — —	„ Sundry Debtors	1 10 5
2121 13 0		Balance Sheet	2209 4 5		550 0 0	„ Loan to General Purposes Account	600 0 0
		Add Excess of Income over Expenditure for			72 8 1	„ Cash at Bank	99 13 6
87 11 5		year	91 19 6				
	2209 4 5			2301 3 11			
	£2222 8 1			£2301 3 11	£2222 8 1		£2301 3 11

The Chemical Society. Balance Sheets, 31st December, 1940.

SPECIAL LECTURES FUND.

1939 £ s. d.	£ s. d.	*Liabilities.*	£ s. d.	£ s. d.	1939 £ s. d.	*Assets.*	1940 £ s. d.
1102 11 11		To Excess of Assets over Liabilities as per last Balance Sheet	1114 18 9		1000 0 0	By Investment as per Schedule (cost or value when acquired)	1000 0 0
— — —					— — —	„ Loan to General Purposes Account	100 0 0
12 6 10		*Add* Excess of Income over Expenditure for year	44 11 10		114 18 9	„ Cash at Bank	59 10 7
	1114 18 9			1159 10 7			
	£1114 18 9			£1159 10 7	£1114 18 9		£1159 10 7

STAFF PENSIONS FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.		£ s. d.
907 14 0		To Excess of Assets over Liabilities as per last Balance Sheet		907 14 0	By Investments as per Schedule (cost or value when acquired)	902 13 9
					„ Cash at Bank	5 0 3
£907 14 0				£907 14 0		£907 14 0

THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.		£ s. d.
1266 0 11		To Excess of Assets over Liabilities as per last Balance Sheet	1162 7 6		By Investments as per Schedule (cost or value when acquired)	1101 7 11
— — —		*Add* Excess of Income over Expenditure for year	50 7 9		„ Cash at Bank	111 7 4
103 13 5		*Less* Excess of Expenditure over Income for year	— — —			
	1162 7 6			1212 15 3		
	£1162 7 6			£1212 15 3	£1162 7 6	£1212 15 3

The Chemical Society. Balance Sheets, 31st December, 1940.

CENTENARY FUND.

1939 £ s. d.	1939 £ s. d.	*Liabilities.*	1940 £ s. d.	1940 £ s. d.	1939 £ s. d.	1939 £ s. d.	*Assets.*	1940 £ s. d.
617 8 0		To Excess of Assets over Liabilities as per last Balance Sheet	778 5 1		750 0 0		By Loan to General Purposes Account	— — —
					— — —		„ Sundry Debtor	3 19 2
160 17 1		*Add* Excess of Income over Expenditure for year	223 6 9		6 16 4		„ Cash at Bank	6 16 4
	778 5 1			1001 11 10	21 8 9		„ Cash on Deposit in Post Office Savings Bank and London Savings Bank	990 16 4
	£778 5 1			£1001 11 10	£778 5 1			£1001 11 10

THE HERBERT SPENCER BEQUEST.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.		£ s. d.
473 7 7		To Balance unexpended at 31st December, 1939	257 7 6		250 0 0	By Loan to General Purposes Account	— — —
		Less Excess of Expenditure over Income for			— — —	„ Sundry Debtor	4 2
216 0 1		year	232 18 0		1 10 2	„ Cash at Bank	1 10 2
	257 7 6			24 9 6	5 17 4	„ Cash on Deposit at Post Office Savings Bank and London Savings Bank	22 15 2
	£257 7 6			£24 9 6	£257 7 6		£24 9 6

THE FARADAY LECTURE FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.		£ s. d.
369 6 8		To Excess of Assets over Liabilities as per last Balance Sheet	380 13 1		369 4 0	By Investment as per Schedule (cost or value when acquired)	369 4 0
		Add Excess of Income over Expenditure for			11 9 1	„ Cash at Bank	23 11 11
11 6 5		year	12 2 10				
	380 13 1			392 15 11			
	£380 13 1			£392 15 11	£380 13 1		£392 15 11

THE TILDEN LECTURE FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.		£ s. d.
1492 2 0		To Excess of Assets over Liabilities as per last Balance Sheet	1878 18 7		1834 10 6	By Investments as per Schedule (cost or value when acquired)	1834 10 6
342 15 9		*Add* Balance of Legacy received from Executors	— — —		44 8 1	„ Cash at Bank	81 18 9
44 0 10		*Add* Excess of Income over Expenditure for year	37 10 8				
	1878 18 7			1916 9 3			
	£1878 18 7			£1916 9 3	£1878 18 7		£1916 9 3

SCHEDULE OF INVESTMENTS.

GENERAL PURPOSES.

Nominal Details.	*Cost or Value when Acquired.*	*Market Value 31st December, 1940.*
	£ s. d.	£ s. d.
£787 London, Midland and Scottish Railway 4% Debenture Stock	839 3 7	783 1 4
£1520 14*s.* 3*d.* Cardiff Corporation 3% Stock, 1914/54	1650 0 0	1414 5 3
£1400 India 2½% Stock	1316 1 0	980 0 0
£2400 Bristol Corporation 2½% Debenture Stock, 1957	2070 2 0	2052 0 0
£2713 London, Midland and Scottish Railway 4% Preference Stock	3572 0 4	1397 3 11
£1200 Leeds Corporation 3% Stock	1143 1 0	966 0 0
£1096 6*s.* 2*d.* Union of South Africa 3% Stock, 1954/64	1067 12 10	1052 9 0
£1200 London and North Eastern Railway 3% Debenture Stock ...	1033 11 0	822 0 0
£3629 6*s.* 9*d.* 5% Conversion Stock, 1944/64	3491 2 8	3910 12 3
£600 4% Funding Stock, 1960/90	480 0 0	684 0 0
£11,426 15*s.* 0*d.* 3½% Conversion Stock, 1961, or after	8874 2 2	11,826 13 9
£408 2*s.* 6*d.* 3% Funding Stock, 1959/69	394 11 5	406 1 8
	£25,931 8 0	£26,294 7 2

PUBLICATIONS FUND.

£5260 19*s.* 9*d.* 3½% Conversion Stock, 1961, or after	3645 12 8	5445 2 5
£3173 1*s.* 6*d.* 5% Conversion Stock, 1944/64	3199 18 7	3418 19 9
£817 P. & O. Steam Navigation Co. Deferred Stock	2060 0 0	878 5 6
£603 London, Midland and Scottish Railway 4% Guaranteed Stock	457 12 7	512 11 0
	£9363 3 10	£10,254 18 8

THE TILDEN LECTURE FUND.

£532 London Transport "B" 5% Stock	625 2 0	553 5 7
186 National Provincial Bank Shares £5 each, £1 paid "B" ...	678 18 0	553 7 0
£220 Metropolitan Water Board (Kent Water Works) 3% Deb. Stock	188 2 0	177 2 0
£376 3*s.* 5*d.* 3% Funding Stock, 1959/69	342 8 6	374 5 10
	£1834 10 6	£1658 0 5

SPECIAL RESERVE FUND.

£800 3% Defence Bonds	£800 0 0	£800 0 0

RESEARCH FUND.

Nominal Details.	*Value or Cost when Acquired.*	*Market Value 31st December, 1940.*
	£ s. d.	£ s. d.
£1000 London and North Eastern Railway 4% 2nd Guaranteed Stock	1010 0 0	610 0 0
£1034 Great Western Railway 2½% Debentures	1049 15 11	630 14 10
£1122 Metropolitan Water Board 3% "B" Stock	1002 16 9	987 7 2
£1483 London, Midland and Scottish Railway 4% Debenture Stock	1508 3 6	1475 11 8
£806 Victoria 3% Stock, 1929/49	706 6 2	773 15 2
£4498 11*s.* 0*d.* 5% Conversion Stock, 1944/64	4267 4 10	4847 3 9
£10,080 5*s.* 5*d.* 3½% Conversion Stock, 1961, or after	8731 10 10	10,433 1 7
	£18,275 18 0	£19,757 14 2

SPECIAL PUBLICATIONS FUND.

£2115 8*s.* 10*d.* 3½% Conversion Stock, 1961, or after	£1600 0 0	£2189 9 8

SPECIAL LECTURES FUND.

£1299 9*s.* 4*d.* 3½% Conversion Stock, 1961, or after	£1000 0 0	£1344 18 11

STAFF PENSIONS FUND.

£683 6*s.* 1*d.* 3½% Conversion Stock, 1961, or after	527 13 9	707 4 5
£371 17*s.* 1*d.* 5% Conversion Stock, 1944/64	375 0 0	400 13 5
	£902 13 9	£1107 17 10

THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

£61 15*s.* 8*d.* 3½% Conversion Stock, 1961, or after	50 1 5	63 18 10
£1255 London, Midland and Scottish Railway 4% Debenture Stock	1051 6 6	1248 14 6
	£1101 7 11	£1312 13 4

THE FARADAY LECTURE FUND.

£374 19*s.* 0*d.* 3½% Conversion Stock, 1961, or after	£369 4 0	£388 1 5

F. P. DUNN, *Treasurer.*

We have examined the above Balance Sheets and accompanying Income and Expenditure Accounts with the Books and Vouchers of the Society, and certify them to be in accordance therewith. We have also verified the Balances at the Bankers and the Investments. Certain figures relating to the Bureau of Chemical and Physiological Abstracts have not yet been subjected to audit by the Auditors of the Bureau and are therefore liable to adjustment.

23, QUEEN VICTORIA STREET, E.C. 4.
13th March, 1941.

W. B. KEEN & Co.,
Chartered Accountants.

PRESIDENTIAL ADDRESS.

Mechanism of the Benzidine Transformation and Some Allied Topics.

By Sir ROBERT ROBINSON, M.A., D.Sc., LL.D., F.R.S.

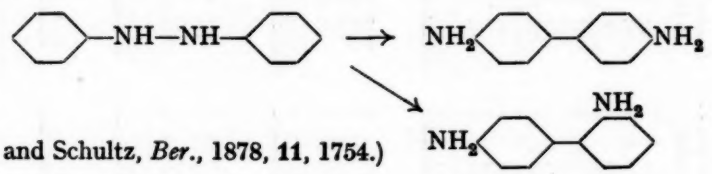
THIS subject has been selected in order to illustrate the thesis that electronic mechanisms should be related not only to all the known facts of a reaction but also to all the relevant analogies.

There are few processes that can be regarded from so many points of view as the benzidine conversion and it therefore provides suitable material for an attempt to develop a more comprehensive symbolisation. The purpose is much wider than appears from the title of this address, because it is hoped that the theory of small electron displacement swings will be found to confer real advantages and that more general use will be made of its resources.

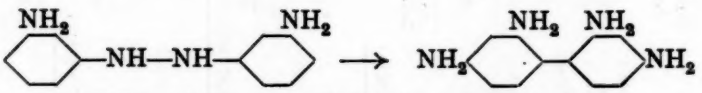
Paul Jacobson, who devoted a large part of his experimental work to the study of the benzidine and semidine transformations of substituted hydrazobenzenes, has published a summary of everything known on the subject in 1922 (*Annalen*, **428**, 76) together with a discussion of the course of the reactions. In view of this it is unnecessary to repeat the historical account and Jacobson's paper should also be consulted for details of the cases examined up to its date. Here we need only the outlines of the chief results. It may, however, be recalled that the discovery of hydrazobenzene and of its rôle as the precursor of benzidine in the reduction of azobenzene (Zinin, 1845) in acid media was announced by A. W. Hoffmann in a communication to the Royal Society in 1863 (*Proc.*, **12**, 576).

The Formation of Diaminodiaryl Derivatives from Hydrazodiaryls.

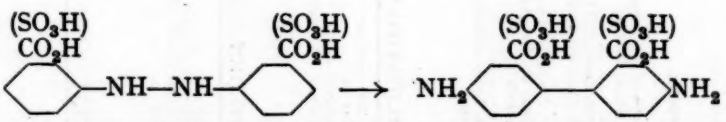
Hydrazobenzenes with free *p*-positions yield *pp'*-diaminodiphenyls and often *op'*-diaminodiphenyls (diphenylines) as by-products:



(Schmidt and Schultz, *Ber.*, 1878, **11**, 1754.)



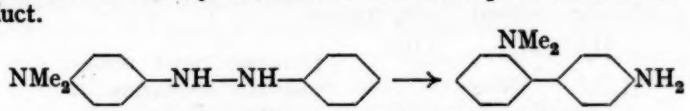
(Elbs and Kopp, *Z. Elektrochem.*, 1898, **5**, 110.)



(Griess, *Ber.*, 1874, **7**, 1610; Mahrenholz and Gilbert, *Annalen*, 1880, **202**, 308.)

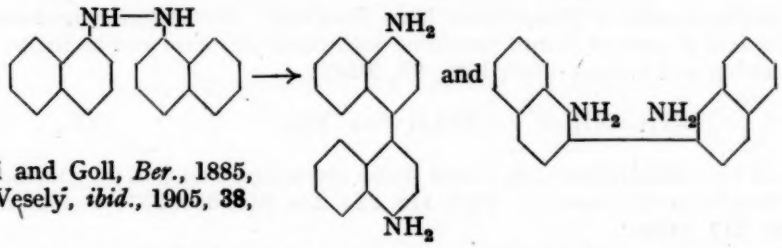
The dicarboxylic acid gives a little diphenyline derivative, the disulphonic acid none. 2 : 2'-Dimethylhydrazobenzene gives a little diphenyline derivative, relatively less than hydrazobenzene; 3 : 3'-dimethylhydrazobenzene affords dimethylbenzidine only (Schultz, *Ber.*, 1884, **17**, 467; Jacobson, *Ber.*, 1895, **28**, 2557). 3 : 5-Dimethylhydrazobenzene also yields a dimethylbenzidine and no diphenyline derivative or semidine (Hönigsberger, Huber, and Jacobson, *Annalen*, 1922, **427**, 204).

In certain cases when the hydrazobenzene bears one *p*-substituent the diphenyline is the chief product.



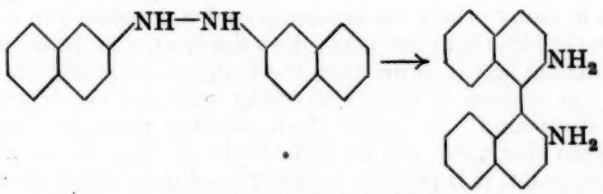
(Jacobson and Kunz, *Annalen*, 1898, **303**, 353.)

Hydrazonaphthalenes may yield 4 : 4′-diaminodi-α-naphthyls, *oo*′-diaminodinaphthyls, or the dibenzcarbazoles derived from these by elimination of ammonia :



(Nietzki and Goll, *Ber.*, 1885, **18**, 3254; Vesely, *ibid.*, 1905, **38**, 136.)

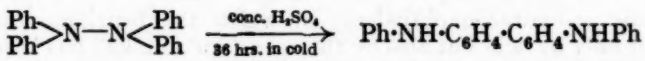
In view of the fact that the 2- and the 4-position show about equal reactivity, it is of interest that no mixed 2 : 4-derivative could be detected in the products.



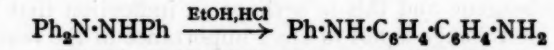
(Meisenheimer and Witte, *Ber.*, 1903, **36**, 4155; Boyd, Dissert., Heidelberg, 1896, mentions a possible *o*-benzidine change in the benzene series.)

There is no record of the formation of a *m*-aminodiphenyl derivative and the orientation of the reaction is exclusively *op*.

The hydrazobenzenes may be *N*-substituted and the reaction succeeds. The following are examples :

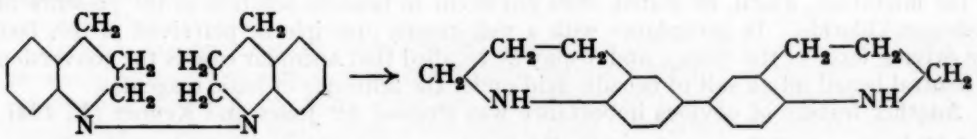


(cf. Gnehm and Werdenberg, *Z. angew. Chem.*, 1899, 1027; Kadeira, *Ber.*, 1905, **38**, 3575; Wieland and Gambarjan, *Ber.*, 1906, **39**, 1499). The main reaction, observed also when hydrochloric acid or acetic acid is employed, is hydrolysis to diphenylamine and the coloured salt of diphenylhydroxylamine.



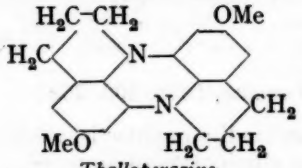
(Busch and Hobein, *Ber.*, 1907, **40**, 2101.)

This reaction is much more facile than that with tetraphenylhydrazine, doubtless because the starting substance is a stronger base and exhibits *less* tendency to dissociate into free radicals.



This transformation (Wieland and Haas, *Ber.*, 1920, **53**, 1336) proceeds smoothly when an ethereal solution of the hydrazine is shaken with 2N-hydrochloric acid. Under similar

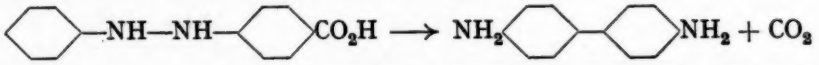
conditions bis-6-methoxytetrahydroquinolyl (*idem, ibid.*) affords 6-methoxytetrahydroquinoline and a substance termed thalloperazine.



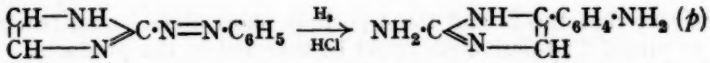
Thalloperazine.

Here we must recognise the formation of an *o*-semidine and its oxidation by the hydrazine derivative.

Certain displacements of groups have been observed. For instance, hydrazobenzene-4-carboxylic acid is converted into benzidine with particular ease and in almost theoretical yield (Noelting and Werner, *Ber.*, 1890, **23**, 2356):



Pyman and his collaborators have shown that a glyoxaline * nucleus may replace a benzene nucleus (Fargher and Pyman, J., 1919, **115**, 222, 238, 244, 250, 257; Pyman and Ravald, *ibid.*, 1920, **117**, 1428):



In this case, as in many others, an azo-compound was reduced in acid solution. We may at once dismiss the idea that there is any deep significance in the simultaneous presence of oxidising and reducing agents, other than the hydrazo-compound, in the system under such conditions. The reagent is always a strong acid and the intermediate is surely always a hydrazo-compound. So many clean reaction processes with pure hydrazo-compounds are known that there can be little doubt of this. Even when the azo-compound is the starting point, it is possible to select conditions which do not encourage the belief that we are witnessing an oxidation–reduction in which the reagents play the part of oxidisers and reducers. For example, azobenzene is smoothly converted into benzidine sulphate by sodium iodide and sulphur dioxide in aqueous solution (Bodenstein, German Patent, No. 172,569 of 1906). The effective reducing agent is hydriodic acid, which is continuously regenerated, and the presence of an oxidising agent, apart from the azobenzene in suspension, is excluded. The point is of some importance because the usual agent, namely, stannous chloride, is converted into stannic chloride, which has some oxidising properties. A case (β-hydrazonaphthalene) in which the benzidine transformation is brought about not only by acid but also by the agency of an alkali has been mentioned by Meisenheimer and Witte (*loc. cit.*). In one place these authors state that they obtain a mixture of products by the alkaline reduction of 2-nitronaphthalene, but they proceed to separate these by the use of hydrochloric acid. However, these authors state in another place that β-hydrazonaphthalene yields 1 : 1′-diaminodi-β-naphthyl on prolonged boiling with alkali. No benzidine or reduced benzidine is formed in the catalytic reduction of azobenzene or hydrazobenzene and this is perhaps an indication that hydrogen *atom* (as distinct from proton) interchange is not of chief importance in the reaction.

It may be assumed with confidence that the transformations are prototropic and occur in a proton-acceptor medium as the result of the action of an acid on a hydrazo-compound.

Tichwinsky (*J. Russ. Phys. Chem. Soc.*, 1903, **35**, 667) was the first to draw attention to the fact that an acid converts a weak base into the salt of a strong base in the course of the migration, which, he stated, does not occur in benzene solution in the presence of hydrogen chloride. In accordance with a well-known principle he perceived in this fact the driving force of the change and it may be recalled that a similar case is the conversion of neutral benzil into a salt of benzilic acid under the influence of basic reagents.

Another feature of obvious importance was stressed by Jones and Kenner (J., 1931,

* Michaelis and Schäfer (*Annalen*, 1915, **407**, 229) have shown that the reduction of 4-benzeneazo-1-phenyl-3-methylpyrazole yields an *o*-semidine (migration of anilino-group) and a *p*-semidine (migration of phenylmethylpyrazolylamino-group).

1848; 1932, 711), who dwelt on the " heterogeneity " of the nitrogen-to-nitrogen link and its tendency to seek relief in dissociation.

The views of A. V. Weinberg (" Kinetische Stereochemie," Brunswick, 1914, p. 70) and of Jones and Kenner are not very different in that they both postulate dissociation of the *salt* of hydrazobenzene into radicals and their subsequent recombination. Tichwinsky, on the other hand, gave the scheme :

$$\begin{matrix} C_6H_5\cdot NH \\ C_6H_5\cdot NH \end{matrix} + 2HCl \longrightarrow \begin{matrix} {}^{-}C_6H_4\cdot NH_3Cl \\ {}^{-}C_6H_4\cdot NH_3Cl \end{matrix} \longrightarrow \begin{matrix} C_6H_4\cdot NH_3Cl \\ C_6H_4\cdot NH_3Cl \end{matrix}$$

A similar theory is that of Stieglitz (*J. Amer. Chem. Soc.*, 1903, **25**, 62), which is represented as follows :

$$Ph\cdot NH\cdot NHPh + HCl \longrightarrow Ph\cdot N< + Ph\cdot NH_3Cl$$

$$Ph\cdot N< \longrightarrow >C_6H_4{:}NH$$

$$NH_2\cdot C_6H_5 + C_6H_4{:}NH \longrightarrow NH_2\cdot C_6H_4{-}\overset{H}{C}{}_6H_4{:}NH$$

$$Ph\cdot NH{-}\overset{H}{C}{}_6H_4{:}NH$$

Semidine

Benzidine

The powerful argument advanced by Jacobson (*loc. cit.*) against this " dissociation " theory in any of its forms is that in 63 examples of benzidine and semidine rearrangements of unsymmetrical hydrazo-compounds, he did not encounter a single case where A–B furnished any A–A or B–B. This proves conclusively that no " mixture " occurs of the aromatic residues contained in a single molecule and it should be noted that the circumstances in some examples are favourable for the recognition of by-products. Thus no benzidine is obtained in the reduction of azobenzene-2-carboxylic acid (Paal, *Ber.*, 1891, **24**, 3060; Jacobson, *Annalen*, 1909, **367**, 328). This was later reinforced by Ingold and Kidd (J., 1933, 984), who made the somewhat similar point that a mixture of 2 : 2′-dimethoxy- and 2 : 2′-diethoxy-hydrazobenzidines gave on conversion a product that behaved thermally as if it contained only the two symmetrical benzidines in the anticipated proportion. The two hydrazo-compounds were found to undergo conversion at comparable rates, the transformation of the dimethoxyhydrazobenzene being very roughly six times as rapid as that of the diethoxyhydrazobenzene.

The transformations of hydrazobenzenecarboxylic acid and benzeneazoglyoxaline (*v. supra*) are difficult to reconcile with any form of a free-radical hypothesis.

Wieland (*Ber.*, 1915, **48**, 1098) also rejected this type of view for the oxidation–reduction of hydrazobenzene with formation of aniline and azobenzene, again because he noted no " mixing " of the radicals in the products.

A further point is that tetraphenylhydrazine dissociates into stable radicals which do not, so far as is known, pass into diphenylbenzidine, even in the presence of hydrochloric acid and yet it undergoes the benzidine change to some extent in sulphuric acid solution (*v. supra*). The plea (Jones and Kenner) that the radicals set free from a single molecule may not escape from the sphere of each other's reactivity does not seem valid here. The weight of evidence is clearly in favour of the true intramolecular character of the migration, because this supplies the only satisfying explanation of the fact that the two nuclei invariably hold together.

Indeed, Jacobson actually investigated a claim by Hirsch (*Ber.*, 1890, **23**, 3222) that he was able to isolate a monomethylbenzidine by conversion of a mixture of hydrazo-compounds prepared by joint reduction of nitrobenzene and *o*-nitrotoluene. It was found (*Ber.*, 1895, **28**, 2545) that even under these conditions benzidine and tolidine only are obtained.

Dr. W. A. Waters has kindly contributed (private communication) a discussion of the

limiting conditions for thermal dissociation in solution. He concludes that dissociation into free radicals is possible if $2\alpha/Dr^3f^2 > 1$, where α is the bond polarisability, D is the dielectric constant, r is the sum of the atomic radii, and f is the covalent bond force constant (cf. Sidgwick, "Chemistry of the Covalent Link," 1933, p. 123). D is clearly the limiting experiment variable. For example, for C–Cl, free radical dissociation requires that $D < 24$, and such dissociation in water is therefore excluded.

Solvents of low dielectric constant are requisite for free-radical dissociation in most cases and this theoretical deduction is in good agreement with experiment.

The obvious features * of the transformation may be summarised as follows:

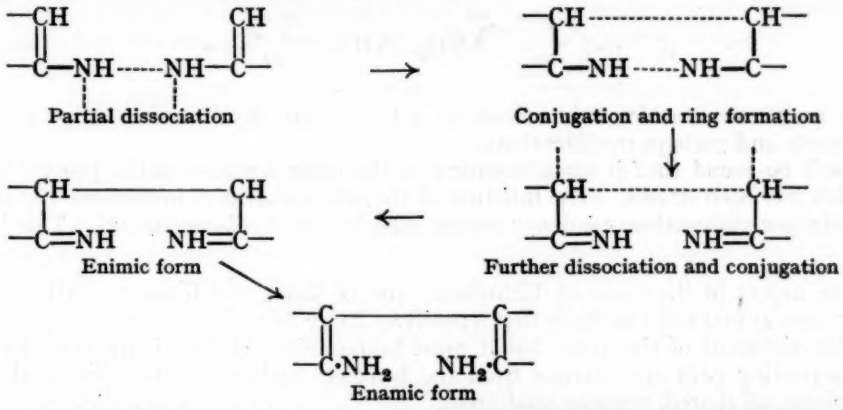
The hydrazobenzene–benzidine conversion is an intramolecular process of oxidation–reduction, because, as pointed out by Jacobson, the hydrazo-group is reduced and the *o*- or *p*-positions of the aromatic nuclei are oxidised. It is brought about by strong acids in a proton-acceptor medium and is therefore probably prototropic. The "heterogeneity" of the hydrazo-group must be recognised in any satisfactory description of the mechanism.

From time to time hypotheses involving intermediate stages have been advanced. *p*-Aminodiphenylamine is certainly not an intermediate, because this base is unchanged by hot mineral acids (Robinson and Robinson, J., 1918, **113**, 643). Lapworth (J., 1898, **73**, 451) suggested that interchange of the anilino-group and hydrogen gives successively the *o*-semidine and *p*-semidine, and that wandering of aminophenyl then gives the diphenyline and the benzidine. The qualification of this hypothesis is best quoted. "The two changes thus represented, however, must probably be regarded as simultaneous and not successive, and it is not suggested that paramidodiphenylamine is actually an intermediate compound, although the latter would probably yield benzidine under suitable treatment." Presumably this difficult passage means that the stages occur in such rapid succession that they are effectively simultaneous. Chattaway (*P.*, 1902, **18**, 176) and Fry (*Z. physikal. Chem.*, 1911, **76**, 397) have also contemplated the semidines as intermediates in the benzidine conversion, and van 't Hoff ("Ansichten," II, 258) thought the intermediate might be 4-hydrazinodiphenyl. These suggestions are not supported by experiments on the supposed intermediates and the value of such experiments was sometimes discounted in advance; they offer no advantages at the present time in the generalisation of the phenomena.

The modern tendency is to avoid the postulation of definite intermediates and to take as direct a view of each change as is possible. The development from this standpoint may now be considered. Employing the symbolism of partial polar dissociation of valency bonds, Robinson and Robinson in 1918 (*loc. cit.*) represented the intramolecular mechanism as a regrouping of polar valencies and a citation from the paper will best serve to make the views of that period clear. "The following brief statement expresses the form in which this and related reactions may be generalised. In a molecular complex A–b–c–D, b or c or both represent atoms capable of assuming a higher valency by salt-formation. The salt absorbs energy and passes into an activated condition,† represented by $\overset{\vdots}{A}—b\cdots\overset{\vdots}{c}—D$, omitting the acid for reasons of convenience. If the partial valencies become conjugated with unsaturated groups in A or D, we obtain $\overset{\vdots}{A}—b\cdots c—D$ and $A—b\cdots\overset{\vdots}{c}—D$. Ring-formation by the partial valencies, followed by a second similar complete process, leads in the first case to b—A—c—D and in the second to b—A—D—c. The products are obtained in the keto-, enimic, or thioketo-modifications, according as the atoms b and c are oxygen, nitrogen, or sulphur. The less extensive change is represented by the semidine transformation, the conversion of phenylhydrazine into *p*-phenylenediamine, of phenylnitroamine into nitroaniline, and by many other reactions. The full change resulting from conjugation of the partial valencies with both unsaturated groups A and D is represented by the benzidine rearrangement, and it is obvious that even within the four corners of the general scheme the nature of the products may be considerably varied according as the conjugated chains in A and D are long or short. The type of rearrangement assumed

* Stereochemical problems are not discussed here, though doubtless of great interest. It seems that the various reactive centres must in any case be near enough to enable the new bonds to be produced. If we are surprised by this, the only course open is to accommodate our ideas to the facts.

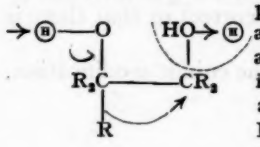
to occur in the synthesis of indole derivatives is represented below, and the thickened lines stand for a normal valency plus a partial valency.



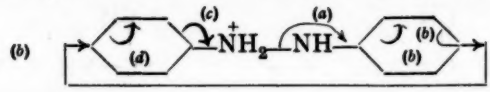
† The activated molecules are said to be ' partially dissociated ' because the phenomenon appears to be a stage towards complete ionic dissociation, but the physical basis of the process is not quite clear. It may be that the energy change causes the movement of an electron from one atom to another (polarisation of the molecule) or a mere change in the position of one or more electrons within the sphere of the atom itself. In this case the evidence shows that the change is repeated in the same sense in alternate atoms forming part of a conjugated chain and in the opposite sense in the other atoms of the chain. Several further suggestions might be made, especially that a part use may be made of the field surrounding a single electron."

It must be emphasised that our dissociated valencies were from the first definitely assumed to be of opposite polarity: $A—B \longrightarrow \overset{+}{A}\,\vdots\,\overset{-}{B}$ and when an electronic basis was more clearly defined the translation $A—\overset{\curvearrowright}{B}$ was suggested * (Kermack and Robinson, J., 1922, **121**, 440) and stated to be applicable to migration mechanisms previously represented with the aid of partial valencies.

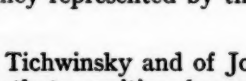
* The curved arrow symbol for an electron displacement was first given in this paper of 1922 (p. 433); it was adopted in teaching from that time on and partial valency representations were abandoned in 1923—1924. Publications in which the system was clearly explained and consistently used appeared in 1925 (*J. Soc. Chem. Ind.*, **44**, 456; J., 1610, 1619; also letters to *Chemistry and Industry* in 1923—1925; Rapport Institut International Solvay, 1925). These earlier papers contained many of the suggestions collected and amplified by Allan, Oxford, Robinson, and Smith (J., 1926, 401). The statement of Wallis (" Organic Chemistry," Gilman, 1938, p. 789) that the present writer " prefers " partial valencies to electronic displacements for the representation of the mechanism of migrations is therefore not correct for the time since 1922—1924. In particular Kermack and Robinson (*loc. cit.*, 1922) mentioned the general form of the pinacol–pinacolin and Wagner–Meerwein changes as examples of reactions which must be represented by electronic displacements equivalent to the polar partial valency symbols previously used. The translations were not published in all cases because they were deemed to be unambiguous. They were, however, given in lectures in several centres in this country, including London, Cambridge, Oxford, and Manchester. The cases chosen always included the pinacol–pinacolin change and, for example, before the Cambridge University Physical and Chemical Society (Jan. 28th, 1926) the representation given was that annexed. The idea that, instead of water being split off from H and OH inside the molecule, a proton comes in from outside and is ejected from another place was adopted at the suggestion of Professor Lapworth in 1924. Lapworth had long since developed similar views in connexion with tautomerism. This modification is the only one that needed to be made in the literal translation of the polar partial valency symbols of 1920. A further point worthy of mention is that the gradualness of migrations and indeed of all bond changes was emphasised by the writer in 1920 (*Mem. Manchester Lit. Phil. Soc.*, 1920, **54**, 4). The words used were: " . . . all the alterations of valency are progressive . . . and a similar gradual change will be found to be true of all the valency rearrangements . . . all these reactions could be regarded as being almost continuous and with many intermediate phases."

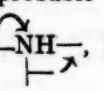


Thus the translation of the above scheme in electronic symbolism became the following for the benzidine rearrangement, and this was given by Ingold and Kidd (*loc. cit.*) :



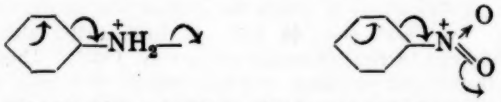
We may now examine this scheme in a little more detail and attempt some small refinements and perhaps modifications.

It will be found that it already embraces the main features of the process to which attention has been drawn. The function of the acid catalyst is to increase the nitrogen-from-nitrogen dissociation tendency represented by the displacement (*a*). This is in line with one aspect of the views of Tichwinsky and of Jones and Kenner  . It may seem at first sight unlikely that a positive charge on a nitrogen atom should facilitate the relinquishment of electrons, but it must be remembered that there is by hypothesis a compensating gain of electrons from the benzene nucleus, so that the total electron atmosphere, all shared, remains unaltered.

It is probable that the process (*a*) should be sub-divided as in the expression :  , but these two displacements may always be combined in a single symbol.

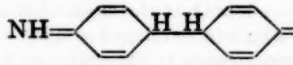
The displacements (*b*) are the usually assumed consequences of the increase of covalency between the nitrogen atom and the nucleus, conferring anionoid * reactivity on the *p*-carbon atom and controlling the orientation of the process. In this part it is merely a normal *p*-substitution of an aniline derivative (hetero-enoid system) by a cationoid reagent (Hamilton and Robinson, J., 1916, **109**, 1029; Robinson, *ibid.*, p. 1038; Robinson and Robinson, J., 1917, **111**, 958; Robinson, *J. Soc. Chem. Ind.*, 1925, **44**, 456; Allan, Oxford, Robinson, and Smith, *loc. cit.* and later papers).

The displacements (*c*), (*d*) require more justification because they are not familiar in hetero-enoid systems and aniline derivatives, even as salts, do not in general display cationoid reactivity. However, the circumstances are sufficiently exceptional and there is a close analogy with nitrobenzene which goes far to justify the assumption made.



It will be observed that in both cases the nitrogen is positively charged and, still more significant, in both cases the nitrogen atom is represented as relinquishing a part of its electron atmosphere. It is hardly necessary to recall the instances of *p*-attack of nitrobenzene by anionoid reagents, because attention has frequently been directed to the examples (*locc. cit.*, 1925, 1926; cf. Bradley and Robinson, J., 1932, 1254). Examination of the details shows, therefore, that the electronic translation of our theory of 1918 is in accord with analogies and expresses many of the features of the benzidine transformation in an acceptable manner. This does not mean that it is necessarily correct or that there is nothing more to say.

We stated, for example, that the product would be obtained in the enimic modification,



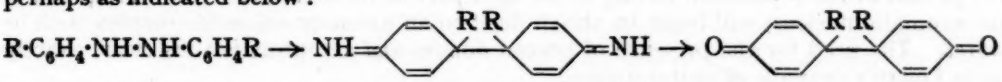
and implied a subsequent tautomeric (prototropic) change in order to reach the benzidine

* The terms "anionoid" and "cationoid" were employed by Lapworth (1925) to denote reagents or reactive centres exhibiting reactivity analogous to that of anions and cations respectively. From the first they had nothing to do with ionic charges and implied "electron donor" and "electron acceptor" respectively. Ingold's terms "nucleophilic" and "electrophilic" are very acceptable alternatives, but the meaning is precisely the same.

salt. This is indeed a necessary consequence of the above electronic scheme if it is taken to the end. Against this idea two strong arguments may be advanced.

In the first place such imine salts are known to be extremely prone to hydrolysis to ketones (later phenols) and yet the production of ammonia or phenols has not been observed even as small by-products.

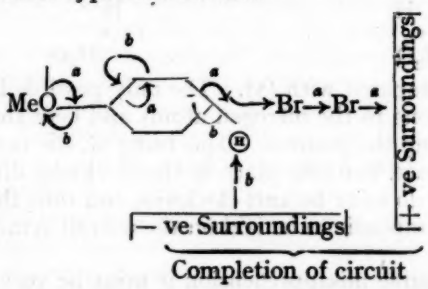
Secondly, this mechanism should operate with *pp*-disubstituted hydrazobenzenes, perhaps as indicated below:



In practice this never occurs; if the *o*-positions are free, a semidine is produced, and hydrazomesitylene, in which there are no free *o*- or *p*-positions, undergoes no rearrangement. Hence it seems certain that the protons in the *p*-positions of the benzene nuclei are removed in the course of the rearrangement, and it is probable also that the nuclei at no time depart far from their aromatic character and never so far that they could be described as hydroaromatic.

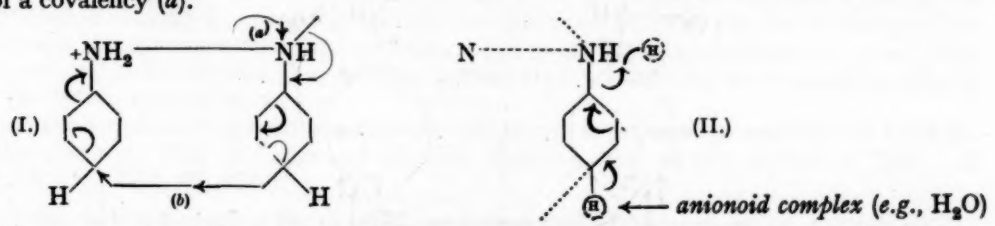
In order to cope with this type of difficulty in similar cases the writer has suggested that many electronic mechanisms are brought to completion by a number of displacement swings or oscillations in different directions, and that each of these may have a very small amplitude. Thus the original activating and orienting displacements are regarded as creating a strain which is relieved by a reversal of only a part of them, the formation of certain new bonds and the breaking of others being progressive though not necessarily unidirectional.*

In aromatic substitution the outcome is that "reaction at a point" which was first regarded as a desideratum by Flürscheim. An example already given is the bromination of anisole [*Chem. News*, 1926, **133**, 3455, 7; "Outline of an Electrochemical (Electronic) Theory of the Course of Organic Reactions," Institute of Chemistry Brochure, 1932, p. 39] and this may be reproduced here, but it must be emphasised that analogous schemes are postulated in all cases of aromatic substitution whether by anionoid or cationoid reagents and in many other types of reactions.



The arrows (*a*) represent a forward process of substitution or addition, whilst the displacements (*b*) relieve the strain in the electromeric system without reversing the effective substitution or addition, accomplished in the first phases.

Applying this to the above electronic mechanism for the benzidine change, we have as the first phase the following (I), in which the arrows represent displacements of unknown and possibly very small extent compared with a full one-electron make or break of a covalency (*a*).



* Because the electrons participating in a new covalency may come first from one side and then from the other, and similarly for the destination of electrons in the breaking of a bond.

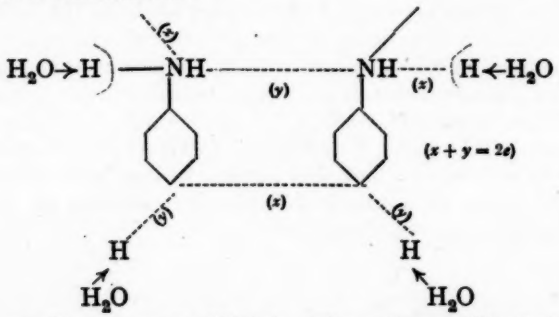
Here the changes not to be reversed are (*a*) and (*b*), for these represent respectively a link broken and a new one formed in the process.

In the next phase the reversal in the right hand nucleus is just the same as that assumed above in the bromination of anisole. It is represented by (II). It is obvious that because of its accumulation of unshared electrons the nitrogen atom will presently take up a proton, and later still one more proton to give the neutral salt of the di-acid base. Furthermore, the proton in the *p*-position, having given up a part of its shared electron atmosphere to the aromatic nucleus, will begin to attach itself to an anion or anionoid complex such as water. The need for the presence of proton donors *and* acceptors is thus clear, exactly as in Lowry's example of mutarotation.

In the left-hand nucleus the displacements are of the same type and are not properly reversals, although by virtue of their occurrence this aromatic nucleus also recovers its original condition.

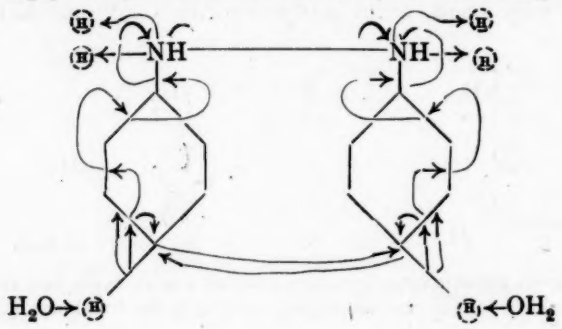
They are expressed in the inset. The same consequences follow, that is, at some stage the nitrogen will acquire a third proton and the proton in the *p*-position will be detached.

Now if we examine the position after these two phases, which it must be reiterated may be assumed to be of extremely small magnitude relative to an electron link, it is noticed that there is no difference between the two nuclei. We have such a condition as :



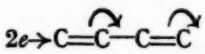
in which (*x*) may be small compared with (*y*). The only possible lack of symmetry concerns the attachment of protons to the nitrogen atoms and here there may well be interchange or resonance levelling up the position. This being so, the next displacement phase, the third we have assumed, need not take place in the clockwise direction represented on paper for the first. It might do so or be anti-clockwise and thus the theory of small successive displacements allows emphasis to be laid on the overall symmetry and gradualness of the change.

In order to avoid any possible misapprehension it must be very clearly stated that it is maintained that each of the phases occurs in detail as already described. The treatment that follows is a simplification that brings out a further aspect of the mechanism. Let it be assumed that clockwise and anti-clockwise displacements alternate with those necessary for *p*-proton removal; then, omitting the displacements which are reversed, that is, those that simply swing to and fro, we arrive at the following representation :

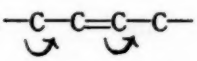


Now this expresses very clearly the intramolecular oxidation–reduction stressed by Jacobson (*loc. cit.*). The hydrazo-group is here seen to be reduced by electrons that pass through * the conducting aromatic nuclei and the *p*-positions are oxidised at the same time, since they lose not two protons merely but a total of two electrons also, that is, two hydrogen atoms. The theory of small displacement swings has thus given us a picture of a symmetrical process which has the closest resemblance to the most direct representation that could be devised.

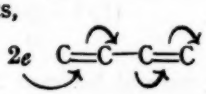
A similar treatment can be applied to the case of graphitic conduction, or conduction in any unbroken unsaturated chain (conjugated double bonds). The mechanism here is



followed by



and, if we sum these displacements,



Thus electrons can enter and leave an unsaturated chain at any point without disturbance of the structure and we avoid awkward assumptions of oxidised or otherwise modified terminal groups. Dr. L. E. Sutton has kindly drawn the writer's attention to the evidence that the benzene ring is a super-conductor and the relation of this idea to its abnormal diamagnetic susceptibility.

Having reached this stage, we are in a position to collate with our view of the benzidine transformation another group of reactions, namely, the oxidative couplings of aromatic nuclei, especially such as occur in the *op*-positions to a hetero-atom (N, O, S). Familiar examples are the oxidation of the naphthols to dinaphthols, the oxidation of dimethylaniline to *N*-tetramethylbenzidine, and the action of bromine on ethyl sodioacetoacetate (which is an oxidation and not an alkylation). It is first necessary to discuss the constitutional factors that make such oxidative couplings possible. In particular we must enquire whether the hetero-atom must bear a hydrogen atom. In the case of the phenols this structural condition certainly must be satisfied, at least when the normal oxidising agents are employed. The phenol ethers are not, for example, oxidatively coupled by chromic acid or ferric salts. On the other hand the disubstituted anilines do undergo the reaction and there is evidence available that it does not occur as the result of salt-formation. Thus strychnidine and many similar bases give intense colour reactions with ferric chloride, due in the first instance to oxidative coupling *para* to the tertiary nitrogen. The reaction occurs in dilute acid solution, but as the concentration of acid is increased the speed of colour formation is diminished and in some cases no colour is developed unless the acid concentration is low. The strychnidine derivative can then be recovered unchanged.

If the analogy of all these processes is conceded, the conclusion must be that the hydrogen atom is *not* an essential structural feature. Had we reached the contrary view, the oxidative couplings might have been formulated as benzidine-type transformations of intermediate hydrazo-compounds and peroxides, and such a mechanism cannot be certainly excluded; it is probably rare but remains a possibility. The rôle of the hydrogen atoms of the phenols is therefore, probably, as in many substitution reactions, to be found in potential or actual ionic dissociation, thereby greatly enhancing the anionoid reactivity of the hetero-enoid system.

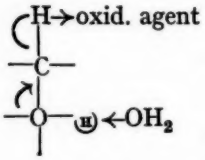
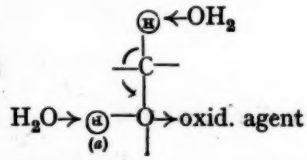
A similar phenomenon among nitrogen compounds is perhaps the oxidation of benzeneazonaphthionic acid to Congo-red (German Patents, Nos. 84,893, 88,595 of 1896; cf. Brass, *Ber.*, 1912, **45**, 2529).

* The electron does not, of course, really pass through such a chain of atoms. A simple mechanical analogy is a row of billiard balls in contact against a cushion where the impact of a ball at one end causes a ball from the other end to move away.

This interesting type of oxidation does not occur with azobenzene but only with those amino- or hydroxy-azo-compounds that are, or may be, formulated for other reasons as arylhydrazones. Here we may be dealing with proton-removal or with the appearance of the more reactive aniline derivative in the form Ph·NH·N=.

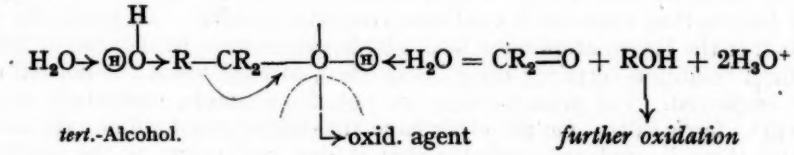
There remains for consideration the question of the position of attack of the oxidising agent. Do the electrons leave the molecule from carbon or oxygen (or nitrogen)? An answer can only be obtained after a study of oxidation mechanisms generally and a digression must be made for this purpose.

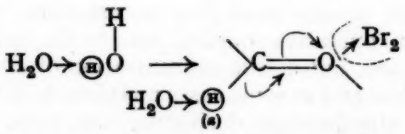
If we take one of the simplest cases, $-CH\cdot OH- \longrightarrow -CO-$, two mechanisms are theoretically possible:

(III.)  and  (IV.)

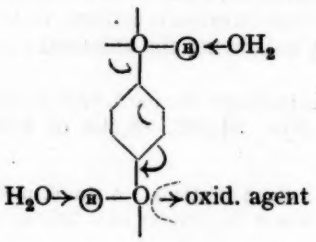
The second alternative is the more natural because the unshared electrons are at once available and because the term " anionoid complex " connotes " reducing agent." The importance of the " consequent process " is clear here, for the reaction succeeds because a condensation of the electrons is possible in the double bond. (The hydroxyl radical has no such convenience and water is not readily oxidised for this reason. On the other hand, water may serve to transmit an oxidation process by the formation of hydroxyl and reduction to water again.) Again it is only the mechanism (IV) which enables a large number of oxidations of organic compounds to be viewed from a single standpoint. If the proton marked (*a*) displays a tendency to ionise, the reducing potential of the oxygen atom is naturally greatly enhanced (hydroxyl ion is a stronger reducing agent than water).

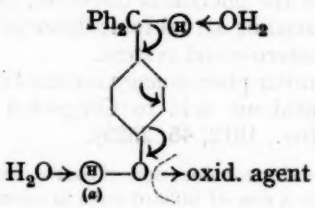
The following is a mixed batch of suggested mechanisms, in all of which the electron leak is from the oxygen atom and there are obvious analogies among nitrogen and sulphur compounds.





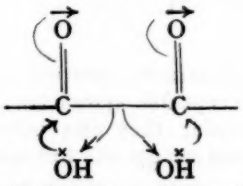
Mechanism (III) would be very unsatisfactory here. The oxidation of a ketone is more difficult than that of an aldehyde because the proton (*a*) is not available for ready detachment. When it occurs, it will be similar to the oxidation of a *tert.*-alcohol. Although every student of organic chemistry knows these facts, the relation between them, so far as the writer is aware, has not previously been discussed.



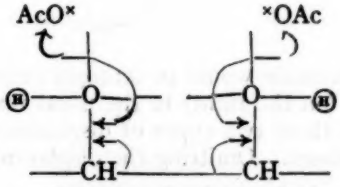


In the oxidation of quinol to benzoquinone one electron may be derived from each oxygen atom and this is probable when the oxidising agent is an acceptor of one electron, *e.g.*, $Fe^{+++} \longrightarrow Fe^{++}$. In the second figure we have a type represented by the direct oxidation of leucoaurin to aurin and again one electron may be derived from each of two centres. The greater the resonance energy of the product, the more facile is the oxidation process and in the nitrogen analogues the proton (*a*) is not detached but instead a distributed positive charge is assumed by the nitrogen atoms.

Quite a different class of oxidations is that by hydrogen peroxide, lead tetra-acetate, and the like. In agreement with Haber these reagents are best regarded as sources of hydroxyl (acetoxyl, etc.) radicals.

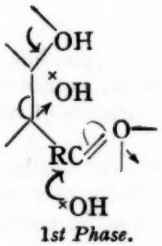


Oxidation of an α-diketone by hydrogen peroxide.

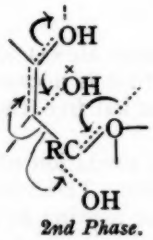


Oxidation of a glycol by lead tetra-acetate.

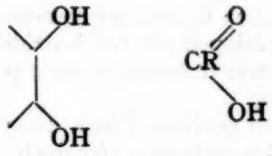
In Dakin's reaction we see the attack of a cationoid centre as above and also an anionoid centre. The latter functions alone in the *op*-hydroxylation of phenols by means of persulphates.



1st Phase.

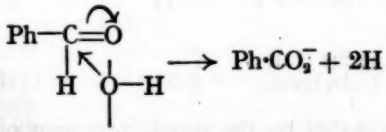


2nd Phase.



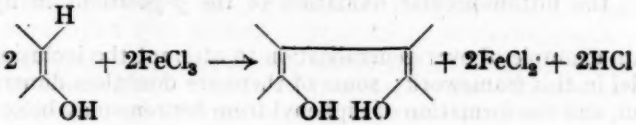
Products.

In this representation of Dakin's reaction the phases are for simplicity transfers of one electron. The use which it is found necessary to make of both unshared electrons and electron defect on different carbon atoms is strong evidence of the free-radical character of the oxidising agent. A third class of oxidation–reductions may be briefly mentioned in passing:

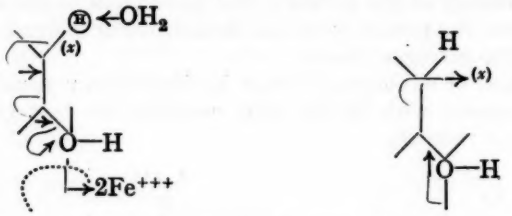


The initial product in the Cannizarro reaction loses two hydrogen atoms in order to become the ion of a carboxylic acid. The benzil–benzilic acid conversion has been discussed by the writer from the same point of view (*Ann. Reports*, 1923, **20**, 118). In the Pondorff and Oppenauer reactions, which resemble the Cannizarro reaction formally, it is possible that both ketone and alkoxyl (or even alcohol) are co-ordinated with the aluminium atom and that intramolecular oxidation–reduction occurs in the complex.

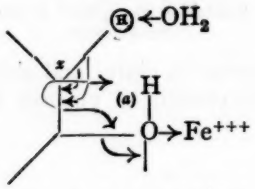
Returning to the case of oxidative coupling of phenols and amines, we take as an example the oxidation of β-naphthol by means of ferric chloride:



It will be agreed that the process is most likely to be symmetrical and that the new bond connecting the aromatic nuclei is not completed as a co-ordinate link. Supposing for the sake of argument that it were so formed, it would be necessary to denude the *o*-position to the hydroxyl of electrons (loss of H^-). The natural scheme for this would be :—



Such a molecule would be strongly cationoid at *x* and would attack a normal β-naphthol molecule (on the right) in the usual manner. The more acceptable symmetrical process combines these two types of displacement in a single molecule; they may occur in successive phases. Omitting the displacements that are reversed we get the following :

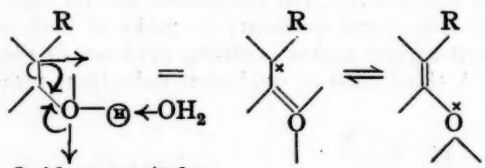


The arrows represent the eventual transfer of one electron each and the two at (*a*) belong to different phases.
Coupling of two *x* positions is possible, due to electrons unshared and in defect.

If two such figures are combined, we get an expression almost identical in principle with that developed for the benzidine conversion. All that is necessary for the combination is of course to connect two *x* positions by the arrows left free, the usual process of radical coupling.

When position 1 in a β-naphthol is substituted, oxidation affords the interesting dehydro-β-naphthols extensively studied by Pummerer. These are dimerides of radicals, into which some of them undoubtedly dissociate on heating in solution or in reactions. The simplest scheme for their formation is perhaps :

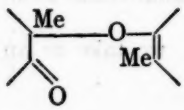
(V.)



Oxid. agent (takes only 1 electron.) (VI.) (VII.)

(VII) is derived from the naphthol by the simple processes of oxidation and removal of proton; the remaining arrows in (V) show the displacements required to pass from (VII) to (VI). Coupling of the electromerides (VI) and (VII) gives Pummerer's preferred constitution, for example, for dehydro-1-methyl-2-naphthol (*Ber.*, 1919, **52**, 1403).

A safe deduction from the fact of the oxidisability of the 1-substituted α-naphthols is that the removal of the proton in position 1 does not occur in the first stages of the oxidation process.



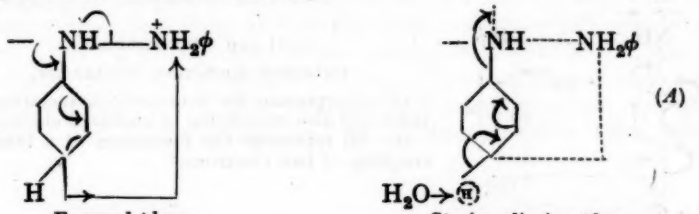
If we have correctly interpreted the facts, the close analogy of these oxidations of the *o*-position in phenols by an external agent with the intramolecular oxidation of the *p*-positions in hydrazobenzene is evident.

It would be an example of over-generalisation to attempt the inclusion of all couplings of aromatic nuclei in this framework; some of them are doubtless dimerisations, followed by decomposition, and the formation of diphenyl from benzene may be so regarded.

*Analogous Theories of the Semidine Rearrangement.**

The semidine rearrangement, like the formation of benzidine, is clearly intramolecular and the arguments mentioned above are relevant to this case also. The conditions of the reactions are like those of the hydrazobenzene to benzidine change and we would expect it to be expressed by a half, or little more than half, of the scheme developed for the full migration. There are, however, several ways in which this can be done.

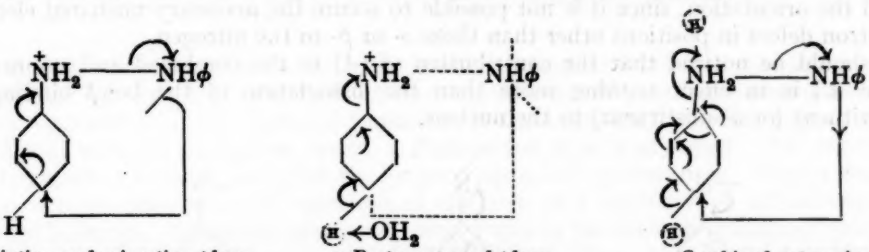
(*A*) Representation as a migration analogous to substitution in which the *p*-position (or *o*-position) exhibits anionoid reactivity.



Forward phase. *Strain-relieving phase.*

Alternation of these phases completes the reaction and in addition the left-hand nitrogen picks up two protons and the right-hand nitrogen loses one proton.

(*B*) A substitution in which the nucleus exhibits cationoid reactivity.



Dissociation and migration phase. p-*Proton-removal phase.* *Combined expression.*

These symbolisations represent the two possible mechanisms in which bonds are eventually broken and new bonds formed unidirectionally. That is, in which two electrons pass from an atom to a neighbour or in which a new covalency is formed by a pair of electrons on one atom becoming associated with the nucleus of another atom.

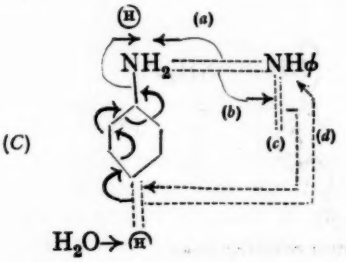
Scheme (*A*) has the advantage that it closely resembles the most acceptable theory of ordinary substitutions of aniline derivatives by means of cationoid reagents (halogenation, nitration, diazo-coupling, etc.). Indeed, if we pursue the obvious analogies of the semidine rearrangement, we are led through the stages : phenylhydrazine to *p*-phenylenediamine, phenylhydroxylamine to *p*-aminophenol, *N*-chloroanilines to nuclear-chlorinated anilines, and perhaps to the migration of diazo-groups in diazoamino-compounds and to the migration of nitroso- and nitro-groups from nitrogen to the nucleus. These reactions exhibit a close formal resemblance and why should the intramolecular nitration by $\cdot NH \cdot NO_2$ in the side chain differ fundamentally from the nitration by $HO \cdot NO_2$?

On the other hand we cannot possibly apply scheme (*A*) to *both* nuclei in the benzidine transformation and (*A*) does not neatly accommodate the function of a strong acid in the semidine change. Although it is hard to allow for the compensating effect of the break of the nitrogen-to-nitrogen bond, we would not expect the appearance of a positive charge in the side chain to enhance anionoid reactivity of the nucleus. Here the *m*-substitution of benzylammonium salts may be recalled.

Scheme (*B*) gives a clear picture of the function of the acid catalyst and it is analogous to one side of the benzidine change (first phase), but the pursuit of the analogies, as detailed above, leads us into conflict with present ideas of aromatic substitutions.

* A *p*-semidine rearrangement is represented, although the *o*-semidine change is much the more common event. This has been done to facilitate ready comparison with the figures in the benzidine section. The group ϕ must be *p*-substituted and might, for example, be $p\text{-}NHAc\cdot C_6H_4$.

It is possible to combine schemes (*A*) and (*B*) and the result is a symbolisation in which the bonds are not broken or formed unidirectionally but are dissociated and produced in a homopolar fashion. As the electrons of a covalency bond do not have the same destination, we represent some of the bonds, not by a line as usual but by two dotted lines; the unshared electrons on one of the nitrogen atoms are similarly represented. Omitting as before the displacements that cancel out in different phases of (*A*), we arrive at the representation below.



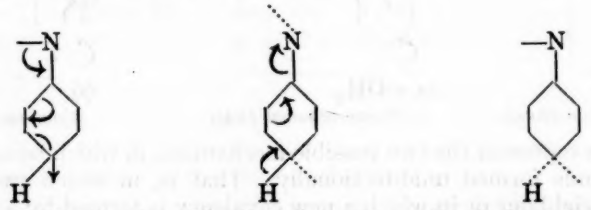
(*A*) and (*B*) combined.

Oxidation–Reduction Mechanism.

(*a*), (*b*) represent the homopolar dissociation of a bond and also regrouping of unshared electrons.
(*c*), (*d*) represent the formation of a bond by coupling of two electrons.*

This expression as it stands supplies no explanation of orientation; a migration to the *m*-position could be represented in the same way. But it is a synthesis of small successive displacements and the first, third, fifth, and so on, of these, of either (*A*) or (*B*) type, control the orientation, since it is not possible to secure the necessary unshared electrons or electron defect in positions other than those *o*- or *p*- to the nitrogen.

It should be noticed that the contribution of (*A*) to the combined and summarised scheme (*C*) is in effect nothing more than the dissociation of the bond binding the *p*-substituent (or *o*-substituent) to the nucleus.



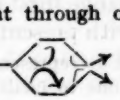
First displacement.† *Second displacement.* *Result of both displacements.*

This will proceed in (*C*) until the dotted lines in the third figure represent one electron each. Every reversible, activating displacement process can be similarly summarised as a dissociating mechanism and, provided the underlying principles are recognised, there is a useful gain in simplification of the figures.

The Orientation Phenomena.

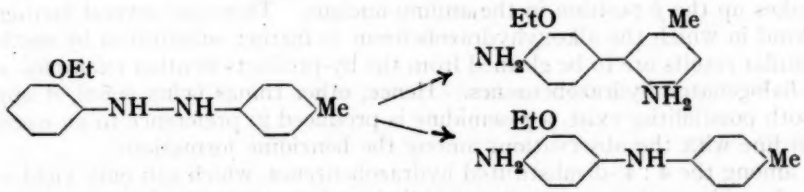
In considering these it must be remembered that a large number of the cases refer to the products of reduction of azo-compounds in acid media, usually by means of stannous

* The contributions of (*c*) and (*d*) to the bond must eventually be equal, one electron each, provided the corpuscular character of the electron persists at this range from the atomic nuclei. It seems just within the bounds of possibility that the conception of the electron corpuscle in the atom, necessarily based on observations of relations with matter and energy outside the atom, may have its origin in a more fundamental quantum property. On the other hand the validity of what we now conceive as a part of a full electron displacement may be denied by physical theory and we should need to replace the conception by one of an equivalent time-variable resonance in the bonds in the course of their making and breaking.

† In this and all similar schemes the displacement through one chain only in the nucleus is represented. This is held to include the possibility  in which the contributions of the two routes may be equal or unequal.

chloride and hydrochloric acid in alcoholic solution. The only exception to the rule that benzidines are formed if the *p*-positions are free appears to be *o*-aminoazobenzene, which gives *p*-phenylenediamine and aniline only (Witt, *Ber.*, 1912, **45**, 2383) and is therefore no real exception. The substituents in the *o*- and *m*-positions may be numerous and varied in nature; they may be neutral, basic, or acidic groups. This fact suggests that the mechanism is of a compelling character and is again hard to reconcile with a free-radical hypothesis—so many different kinds of free radicals have to be postulated and they all need to behave in the same way.

The *op*-coupling to a diphenyl derivative occurs as a side reaction with hydrazobenzene itself (production of diphenyline) and as the main process where one of the *p*-positions is occupied by Cl, Br, I, NMe_2, OAc, NHAc (with CH_3 substituent); NHAc alone leads to *p*-semidine and reduction to simple amines). In other similar cases the *op'*-diamino-diphenyls represent one of the main products and *o*-semidines are also obtained in substantial amount. For example (Jacobson and Huber, *Annalen*, 1909, **369**, 7):

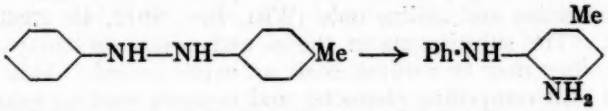


A curious anomaly is that 4-methylhydrazobenzene does not appear to yield a methyldiphenyline but only an *o*-semidine. 4-Hydroxyazobenzene splits up on reduction. The general conclusion is that diphenyl formation is favoured, the benzidine type if possible and if not, with the exceptions noted, a diphenyline type is obtained. The tendency is clearly apparent to bring into play the longer conjugated systems first. This is connected in the writer's view with the question of duration and intensity of activations in the different positions. Attention has already been drawn to the example of diazo-coupling with 1-naphthol-3-sulphonic acid (Lapworth and Robinson, *Mem. Manchester Lit. Phil. Soc.*, 1927—1928, **72**, 45; Institute of Chemistry Brochure, 1932, 42). Here the diazo-salts of lower reactivity attack the *o*-position to hydroxyl, diazo-salts of medium reactivity attack both *o*- and *p*-positions, and diazo-salts of high reactivity (*e.g.*, 2:4-dinitrobenzenediazonium chloride) attack the *p*-positions only. The deduction was that the *p*-positions are less strongly activated than the *o*-positions and so can be attacked only by a reagent reaching a certain high chemical potential. But in order to accommodate the results the stronger activations in the *o*-positions which can make use of reagents of lower chemical potential must be of lower frequency than those in the *p*-positions. Otherwise the product should always be an *o*-hydroxy-azo-compound. Applying this idea to the hydrazobenzenes, it is only necessary to assume that the degree of frequent activation (value of unshared electrons or electron defect) in the longer conjugated systems reaches the level necessary for initiation of new bonding in order to explain the results. A steric factor may operate in addition, particularly if a powerful activation on one side of the hydrazo-group has a high frequency or duration. This is supposed to measure itself against the other side and there induces a reactivity which is not normally exhibited. This consideration may explain the success of Fischer's indole synthesis (cf. Robinson and Robinson, *loc. cit.*) and the interesting fact that α-hydrazonaphthalene affords 1:1'-diamino-di-β-naphthyl and 4:4'-diamino-di-α-naphthyl but not a mixed *op*-αβ-derivative (*v. supra*).

The orientation phenomena among the semidine formation reactions are more varied and give answers to two questions. Which of the anilino-groups of an unsymmetrical substituted hydrazobenzene will migrate, and will it take up the *o*- or the *p*-position in the other nucleus?

The question as to whether *o*- or *p*-semidine formation is preferred is often impossible to answer because the issue is confused by the effect of migratory aptitude. For example, as the anilino-group has a greater migratory aptitude than the *p*-tolylamino-group

(Jacobson, *loc. cit.*), we are here debarred from a comparison of *o*- versus *p*-semidine formation.



This is a case suited better by mechanism (*B*) or (*C*) than by (*A*), because the general electron displacement produced by the methyl group is from right to left and because *p*-toluidine is a stronger base than aniline.

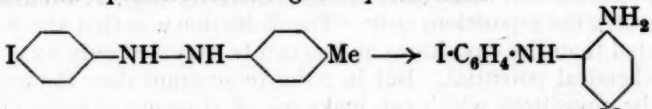
When the single substituent is a *p*-methoxyl or ethoxyl group, we again get as chief product an *o*-semidine in which the anilino-group has migrated. Here the general electrical effect of the OR group is opposite to that of a methyl group, but this is balanced by the electromeric displacement, $\phi \overset{\curvearrowleft}{-} OR$.

However, in these cases the alkoxyphenylamino-group does migrate to some extent and it takes up the *p*-position in the anilino-nucleus. There are several further examples of this kind in which the alkoxyhydrazobenzene is further substituted by methyl groups. A few similar results are to be gleaned from the by-products in other examples, such as the mono-*p*-halogenated hydrazobenzenes. Hence, other things being equal, it appears that, where both possibilities exist, a *p*-semidine is produced in preference to an *o*-semidine and this is in line with the observations among the benzidine formations.

It is among the 4 : 4′-disubstituted hydrazobenzenes, which can only yield *o*-semidines (or the *o*-benzidines observed in the naphthalene but not in the benzene series), that we have the clearest comparisons, but here again the discussion is difficult because the orientations are analogous to those in the substitution reactions of disubstituted benzene derivatives. From individual cases we find the following migratory aptitudes; a few of these do not relate to 4 : 4′-disubstituted hydrazo-compounds. The substituents alone are indicated (for references, see Jacobson, *loc. cit.*) :

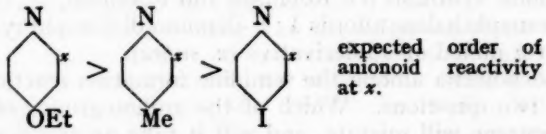
H>Cl; H>Br; H>I; H>Me; H>OMe; H>OEt;
4-OAc-3-Me>Me; NMe_2>Me; NMe_2>OEt; I>Me;
Me>OEt; Me>4-OEt-3-Me; 3-Br>OEt; 4-Br>OEt.

To take one example of the interpretation of this list, I>Me means that the *p*-iodoanilino-group migrates into the *o*-position to nitrogen in *p*-toluidine.



The results do not exactly fit a simple scheme of anionoid or cationoid reactivity of the nucleus and disclose the operation of a complex of factors. If we exclude for a time the case of the anilino-group, there is a short series that can be placed in order : I>Me>OEt, with confirmatory evidence in the case of groups that cannot be included because of the lack of certain direct comparisons.

Here we certainly find that the accepting nucleus is that which possesses the greater anionoid reactivity as judged by known substitution reactions and by general theoretical considerations.

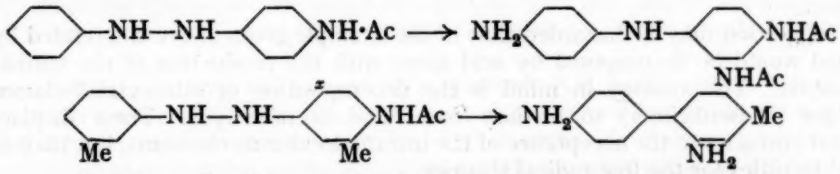


expected order of anionoid reactivity at *x*.

The cases NMe_2>Me and NMe_2>OEt may appear to contradict this, but in a strongly acid solution we have the salt NMe_2H^+, and the expected effect is reversed when we pass from such a base to its salts.

Hence these results are in agreement with *initiation* by mechanism (*A*). Returning now to the anilino-group, the observations H>Me and H>OR are in harmony with the

above but H>hal. seems anomalous. We are justified to a large extent in excluding these cases because of the complexity of the experimental results. Thus 4-chloroazobenzene on reduction in acid solution gives benzidine (by elimination of chlorine), chlorodiphenyline as the main product, anilinochloroaniline (the *o*-semidine), some chloroanilinoaniline (the *p*-semidine), and a part is reduced to *p*-chloroaniline and aniline. In view of the difficulties of the separations it is not possible to give the yields of these products exactly, but it is evidently illogical to concentrate attention on the contrast in the *o*-semidines. The benzidine, chlorodiphenyline and *p*-semidine may be credited to initial anionoid reactivity of the anilino-group. What does appear is that the reactivity of an anilino-group is preferentially displayed in the *p*-position to nitrogen. A special contrast is afforded by the cases



(Jacobson, Jaenicke, and Lockemann, *Annalen*, 1922, **427**, 200.)

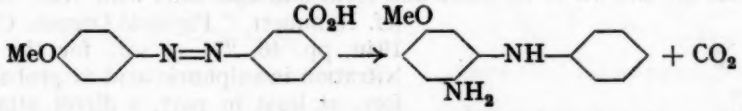
Here the directive effect of the methyl group is strong evidence of anionoid reactivity exhibited in the *p*-position to it (*x*).

The results as a whole favour the view that the initiation is by mechanism (*A*). This, as implied above, is the orienting process. The value of its combination with (*B*) to give (*C*) is the advantage of closer accord with the benzidine conversion itself, the accommodation of more analogies, and the removal of certain disadvantages of a pure (*A*)-type mechanism.

The Displacements accompanying the Formation of Benzidines and Semidines.

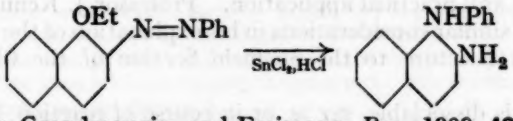
Azobenzene-4-carboxylic acid (Jacobson, *Annalen*, 1898, **303**, 384) and azobenzene-4-sulphonic acid give almost quantitative yields of benzidine on reduction in acid solution under the usual conditions. This is not unexpected, because these groups are frequently displaced quite readily in aromatic substitutions by cationoid agents. Wherever a proton is detachable by a water molecule, the cationoid CO_2H and SO_3H groups may equally be removed, *e.g.*, $-C\overset{O_2H}{\curvearrowleft}\leftarrow O-\overset{H}{\oplus}\leftarrow OH_2$, the products being carbonic acid and a hydrated hydrogen ion. The direct formation of carbon dioxide might also be postulated, but such a scheme would not apply to the elimination of the sulphonic group.

It is stated (Jacobson, Jaenicke, and Lockemann, *loc. cit.*) that 4-methoxyazobenzene-3-carboxylic acid on reduction in acid solution under the usual conditions affords fission products and 2-amino-5-methoxydiphenylamine:



This, if confirmed, indicates a remarkable ease of decarboxylation of the primary product. The elimination occurs in the migrating anilino-group and hence has little bearing on the theory.

Displacements of halogens have been observed in benzidine conversions, of acetoxyl groups in *p*-semidine formations (and in one case in the formation of an *o*-semidine), and of alkoxy-groups in the formation of *o*-semidines. *E.g.*,



(Nölting, Grandmougin, and Freimann, *Ber.*, 1909, **42**, 1378.)

These reactions underline the very great tendency for the occurrence of the migrations; they are overall reductions of the hydrazo-stage and may be compared with the reduction of *o*- and *p*-halogenated amines and phenols and of α-halogenated ketones. The reducing agent is evidently the stannous chloride employed, but, as the reduction of 2-amino-1-ethoxynaphthalene cannot be effected under similar conditions, it is clear that the reaction mechanism facilitates the process. The mechanisms already suggested necessitate the progressive detachment of the OR^+, in which the oxygen atom has only a sextet of electrons. The group will gradually become a powerful oxidising centre as the conversion proceeds and eventually take up two electrons from the stannous ion. It is the converse of the attack of nitrobenzene in the *p*-position by anionoid reagents. Here the hydrogen atom is displaced plus an extra electron (H^-) and this reduces some substance present in the system.

The suggestion may be hazarded that in the example given above the related hydrazo-compound would be decomposed by acid alone with the production of the semidine and acetaldehyde. The analogy in mind is the decomposition of ethoxytrialkylammonium hydroxides (Meisenheimer) to tertiary bases and acetaldehyde. These displacements present no obstacles to the acceptance of the intramolecular mechanisms, but they are very serious difficulties for the free-radical theories.

Possible Repercussion on the Theory of Aromatic Substitution.

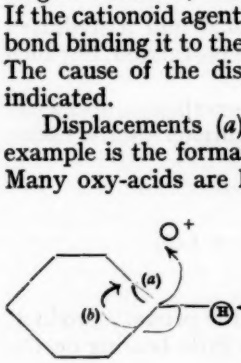
It has been shown that the hypothesis of successive small displacements allows us to combine two mechanisms (*A*) and (*B*) which control orientation (in the same sense) and that in the result (*C*) we achieve virtually non-polar reaction as the consequence of the alternate appearance of unshared electrons and electron defect at one and the same carbon atom. The possibility existed because there was a dissociable and reducible bond (N–N) in the system considered.

On general grounds we would expect a similar process for substitution by an external agent replacing the electron transfer through the nucleus to the reducible bond by a direct transfer of electrons from the site of substitution to a part of the reagent.

There is nothing novel in the results to which this suggestion leads, but the point is included because of its relation with the preceding discussion.

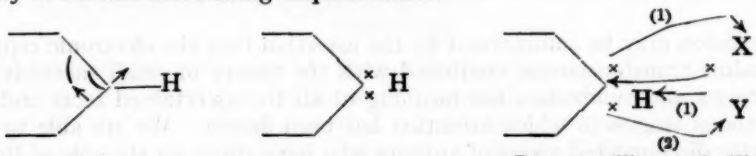
When a hydrogen atom attached to an aromatic nucleus is substituted as the result of attack by a cationoid reagent, the aromatic compound is oxidised and the cationoid reagent reduced; electrons pass from the aromatic substance to the substituting agent. If the cationoid agent is effective as a cation, then it cannot contribute electrons to the new bond binding it to the nucleus and we get a unidirectional process [analogous to (*A*) above]. The cause of the displacement in the nucleus is not specified; only the final result is indicated.

Displacements (*a*) and (*b*) alternate until the substitution is complete. A familiar example is the formation of azo-compounds from amines or phenols and diazonium salts. Many oxy-acids are known to be bases and form ionisable salts with other strong acids (cf. Hammett, " Physical Organic Chemistry," 1940, pp. 46, 271 *et seq.*, for the evidence). Nitration in sulphuric acid is probably, therefore, at least in part, a direct attack on the nitroxyl cation. This consideration explains the remarkable catalytic effect of perchloric acid in sulphonations and nitrations which has been observed in the Dyson Perrins Laboratory by Mr. G. Müller. A mixture of absolute nitric and perchloric acids is capable of effecting difficult nitrations far more quickly and at a lower temperature than one of nitric and sulphuric acids. The process is, however, too dangerous to have any practical application. Professor J. Kenner (private communication) has made use of similar considerations in his explanation of the course of diazotisation in strong acid media (Lecture to the Sheffield Section of the Chemical Society, Feb. 28th, 1941).



But if the reagent is dissociable, *per se*, or in course of reaction, into radicals or atoms

with both unshared electrons and electron defect, the course of the process is perhaps more likely to be (*a*) orienting loosening of the hydrogen to be displaced in accordance with principles already discussed and (*b*) direct oxidation of the substituted position without the necessity of further alternating displacements.

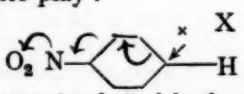


Processes (1) precede (2)

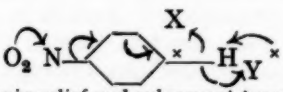
If at any stage the hydrogen is detached as a proton, it is clear that the electron previously binding it to the aromatic nucleus is at once available to reduce an atom or radical to an anion.

The radicals X, Y may be replaced by a molecule XY, which suffers homopolar disruption in the course of the reaction, or X, Y may be derived from different molecules or from different parts of the same molecule. For example, the radicals may be produced by photochemical or thermal activation, from a molecule such as Br_2 or HNO_3 (NO_2,OH) in the course of reaction, or from the decomposition of a substance such as $SbCl_5$ into $SbCl_3$ and 2Cl. The essential point is that the orienting polar displacement may be, and probably is, very small in relation to a full bond formation, and the substitution process may then be completed by homopolar coupling.* The latter is the equivalent with an external reagent of the later phases envisaged for the internal oxidation–reduction characteristic of the benzidine and semidine conversions. This idea fits in with the fact that the efficiency of control of orientation by the directing group in aromatic substitution has no kind of relation with the extent of electromeric displacements in the average resting phase that can be roughly estimated by dipole measurements. Chlorobenzene is nitrated in the *op*-positions as exclusively as phenol. However, when two different electromeric displacements can occur in one and the same molecule, their amplitude will naturally be one factor in control of relative reaction speeds. This may be brought about by the simultaneous appearance of different values of unshared electrons at the two possible sites of reaction or by a time-variability resulting in the more frequent appearance of unshared electrons (or of course electron defect) at the one site or at the other.

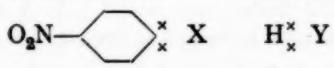
Finally, in agreement with Hey (Grieve and Hey, J., 1934, 1797; 1938, 108; Hey, J., 1934, 1966, and later papers), what is called amphoteric substitution is evidence of the operation of free radicals (cf. Hey and Waters, *Chem. Reviews*, 1937, No. 21). In these cases one and the same agent applied under similar conditions introduces a substituent *op* to either an anionoid group such as NMe_2 or a cationoid group such as NO_2. In a cationoid system it is evidently the electron defect of a carbon atom of the nucleus which is first brought into play :



1*st Displacement and attack by the radical* X.



Strain relief and subsequent processes.



* Ingold and Ingold (J., 1926, 1313) have already proposed a " directive process," followed by a " subsequent change." The directive process for *op*-substitution was identical with that previously suggested by the writer. The " subsequent change " envisaged was a polar mechanism in which the proton from the position nitrated (for example) combined with hydroxyl ion from the nitric acid. This is a limiting case of the unidirectional mechanism (*A*) in which we assume that the proton is extracted by *some* neighbouring anion or anionoid complex. Ingold and Ingold proposed a quite different mode of *m*-substitution, which was regarded as an attack in the first instance on the hydrogen displaced. The writer has never concurred in this view and regards the mechanisms of *op*- and *m*-substitutions as identical in so far as the attack by the reagent is concerned. The orientation phenomena and other circumstances have been frequently discussed.

The suggestion made above is that a substitution oriented and initiated by polar displacement may be completed by a homopolar process. Just as the energy required to separate ionic charges is recovered in a complete cycle, so that required to separate duplets is compensated by the recombination of electrons to form other duplets.

This discussion may be summarised by the assertion that the electronic representation of the benzidine transformation, combined with the theory of small successive displacements, expresses and symbolises the meaning of all the ascertained facts and interprets acceptably the analogies to which attention has been drawn. We are able to harmonise the apparently disconnected views of authors who have dwelt on the rôle of the acid, the medium, the heterogeneity of the hydrazo-group, and the aspect of an oxidation–reduction process. We note also new analogies with orientation in other benzene substitutions and with the oxidative couplings of aromatic amines, phenols, and enols generally.

OBITUARY NOTICES.

ARTHUR GEORGE BLOXAM.

1866—1940.

ARTHUR GEORGE BLOXAM was killed as the result of enemy action on November 7th, 1940, in his 75th year. He was the son of Professor Charles Loudon Bloxam, of King's College, London, and nephew of Sir Frederick Abel. From 1882 he studied Chemistry under his father's successor, Professor J. Millar Thomson, at King's College, and continued there as demonstrator until, in 1887, he became chief assistant to Professor Edward Kinch at the Royal Agricultural College, Cirencester. In 1891, at the early age of 25, he was appointed head of the chemistry department of the Goldsmiths' Institute, New Cross, and, assisted by his cousin, Hugh Charles Loudon Bloxam, who died in July, 1940, made the new establishment an almost immediate success as an evening school for Honours students. His teaching was very thorough, somewhat ambitious for those days, and did credit to the well-endowed laboratories. He prepared the way for the brilliant researches in stereochemistry of his successor, the late Sir William Jackson Pope.

In 1897 Bloxam relinquished academic chemistry in favour of applying his ability to patent law, in which he became an outstanding authority, especially as related to the synthetic dye and chemical industries. He was President of the Chartered Institute of Patent Agents in 1926—1927, having previously served several periods as a Member of the Council of that Institute, and of its Board of Examiners. He was elected an Associate of the Institute of Chemistry in 1887, and a Fellow in 1891, and served as a Member of its Council, 1914—1915. He became a Fellow of the Chemical Society in 1888.

In 1902 Bloxam married Winifred, a daughter of Mr. A. B. Shapland of Barnstaple. They had a son and five daughters, one of whom, Mrs. McCormick, was killed at the same time as her father. Much of his leisure was spent with his family, which was undoubtedly his chief interest in life. He was reserved, but to those who knew him he was a man of strong personality, chivalrous, kind, courageous, and ready to help those who sought his advice or sympathy. His friendship was precious to those who were fortunate enough to enjoy it, to none more, perhaps, than to the writer. He was a keen Churchman on the Evangelical side of the Church of England, and took an active part in the lay administration of the churches with which he was connected. He was a voracious reader, especially of Dickens and the Victorian novelists. He took little interest in any hobby or sport except walking, which helped to foster his delight in the beauties of nature. He had a lively sense of humour.

His experience of the general principles and progress of chemistry was kept fresh by his editing five editions of "Bloxam's Chemistry," first in association with Professor Thomson, and later with Dr. S. Judd Lewis. Many paragraphs in "Bloxam" were contributed by him as an outcome of his experience of modern developments. He edited also "Laboratory Teaching," which reached a sixth edition, and was joint author with the late Mr. Bertram Blount of "Chemistry for Engineers and Manufacturers." Most of his contributions to current literature had reference to patent law and its association with chemical inventions (see *J. Soc. Chem. Ind.*, 1907, 573; 1916, 808; 1919, 324R) and to patents for dyes, etc., detailed in *British Chemical Abstracts*.

S. JUDD LEWIS.

EDWARD HAWORTH.

FRIENDS and colleagues will regret to know that Edward Haworth passed away on June 14th, 1940.

Haworth was born in the Blackburn neighbourhood, and educated at Burnley Grammar School. Thence he went to Owens College, where he graduated and continued as research assistant to Prof. W. H. Perkin, F.R.S.; later he was associated with Professors Dixon and Boyd Dawkins.

In January, 1898, having taken his M.Sc. degree, Haworth joined the staff of the Castner Kellner Alkali Co., Ltd., at Weston Point, Runcorn, under the late Harry Baker, who was formerly a distinguished assistant at Owens to Sir Henry Roscoe. He joined at a most interesting time, as the large-scale electrolysis of brine was then in an experimental stage.

Under Baker's direction Haworth undertook many interesting investigations, amongst which were a salt purification process for which he was later awarded his D.Sc. degree, and subsequently he shared in the development of Castner's sodium process and other processes which the Company investigated. Perhaps his most important work lay in the operation and development of the Mond gas process for the production of electrical energy from generators driven by large gas engines, on the scientific management of which depended the economic success of this process.

Sodium perborate was another of the subsidiary processes developed under Haworth's direction; also he was associated with the development of the only liquid chlorine plant existing in any of the allied countries at the time when the Germans first used poison gas.

Haworth will long be remembered and honoured for the prominent part he took in promoting the welfare of the firm's employees. He subsequently became the first chairman of the firm's highly successful recreation club, which provides amenities of a comprehensive character for both indoor and outdoor games.

Haworth's life was so much occupied with the affairs of the Company that he had no time to devote to other public duties, but his wife, who survives him, was secretary of the District Nursing Association and was the first woman magistrate in the town: his only son is on the staff of Imperial Chemical Industries, Lime Group, and his daughter (Mrs. Lea) also is associated with I.C.I., as her husband is a chemist with I.C.I.'s General Chemical Group.

J. W. Moore.
E. O. Glover.

JOHN WILLIAM TOWERS

1855—1941.

A well-known and popular personality in the chemical industry of Lancashire has passed away by the death of J. W. Towers, who was a Fellow of this Society for nearly fifty years.

Towers was born at Bury on April 6th, 1855. He served an apprenticeship with a pharmaceutical chemist at Southport and later became a student under Professor Roscoe at Owens College, Manchester, after which he entered the laboratory of Messrs. John Hutchinson and Co. at Widnes. Here he was associated with Dr. Ludwig Mond and Mr. (afterwards Sir) John Brunner; in fact he worked at a bench next to that of Dr. Mond and was instructed by him in the tests used in the Mond sulphur recovery process. He was afterwards employed by the Atlas Chemical Co.

In 1882 Towers founded the firm at Widnes which bears his name and which under his guidance was gradually expanded in various directions so that when war broke out in 1914 he was able to supply many of the requirements of chemical industry previously imported from abroad. Meanwhile, he had many inventions to his credit, probably the best known being the Towers Respirator, which was designed for the protection of persons working in atmospheres containing noxious gases and was the forerunner of the gas-mask of today. He was keenly interested in photography and helped to found the Widnes Photographic Society, of which he was the first secretary; he was also a member of the Liverpool Amateur Photographic Association for half a century. In this connection it is interesting to note that he provided Hurter and Driffield with the special apparatus which they used in their researches in photography.

In spite of devoting exceptionally long hours to his business, Towers found time for public duties; he was one of the first members of the Widnes Chamber of Commerce and in 1929 was its chairman; he was also for a time a member of the Lancashire County Council. He was an Original Member of the Society of Chemical Industry and for many years regularly attended the meetings of the Liverpool Section, serving at various times on

the Committee. Members of the Society always welcomed him because of his unfailing cheerfulness; in fact the outstanding characteristics which remain in one's memory are his helpfulness in any matters on which he was competent to advise and his abundant good spirits; the large gathering at the service held in his memory at Allerton, near his Liverpool home, was a tribute to his popularity.

Towers leaves a widow, two daughters and a son, Mr. John Swainson Towers, who is now managing director of the company which his father founded. E. GABRIEL JONES.

FRANK WATSON YOUNG.

1852—1941.

FRANK WATSON YOUNG, whose death in his ninetieth year took place at Farnham on January 10th, was born at Dundee and was educated at the West End Academy, Dundee. He began his career as a "Druggist's Boy" and, showing an early interest in science, attended evening classes when these were instituted in Dundee. He later continued his studies at the Royal College of Chemistry and at the Royal School of Mines.

Young's first appointment was as lecturer in chemistry and physics at Dundee Young Men's Christian Association, where overflowing classes were a tribute to his gifts as teacher and organiser. In 1877 he was appointed first science master at Dundee High School; in this position, which he held for 23 years, he did much to advance interest in science in that city, and when the Technical Institute was founded he became its first Director of Studies. With the late Professor Carnelley, Young founded the Dundee and District Association for the Promotion of Technical Education and was thus brought into close relation with educational authorities in Scotland. In 1900 he was appointed one of H.M. Inspectors of Schools and continued in this capacity until, in 1917, he was entrusted with the organisation and administration of the scheme for the training of ex-servicemen in universities, technical colleges, and training colleges.

Young retired in 1924, and in the following year received the C.B.E. in recognition of the services he had rendered to Education. He was elected a Fellow of the Chemical Society in March, 1877.

FRANK G. YOUNG.

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43. *Tetrachloronaphthalenes derived from Dichloronaphthalene Tetrachlorides and from Trichloronaphthalenesulphonic Acids.*

By (Miss) E. GERTRUDE TURNER and W. PALMER WYNNE.

An account is given of the acids formed by the interaction of the fourteen isomeric trichloronaphthalenes with chlorosulphonic acid. From these products, through the intermediary of the corresponding trichloronaphthalenesulphonyl chlorides, fifteen of the twenty-two possible tetrachloronaphthalenes are described. Of these, the constitutions of seven have been ascertained, and of the remainder the relative position of three of the chlorine atoms has been fixed. Incidentally, from a study of two dichloronaphthalene tetrachlorides an alternative line of approach proved useful in educing the orientation of two of the tetrachloronaphthalenes.

THE programme of work on naphthalene derivatives planned by Armstrong and Wynne during the period 1886—1897 included the sulphonation of the trichloronaphthalenes (cf. Proc., 1890, 11; 1895, 86), but only one communication, that dealing with the products obtained from the two homonucleal isomerides, was published (*ibid.*, 1890, 76), more urgent problems demanding attention during the later years of the collaboration. The sulphonating agent employed by them was 10% oleum at 100°, the weight used being four times that of the trichloronaphthalene—an amount of SO_3 14% in excess of that required for

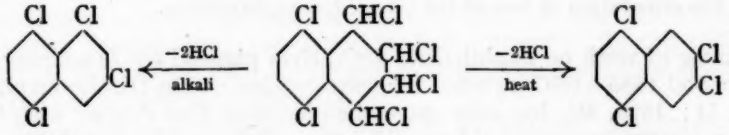
monosulphonation—and the products from the 1 : 2 : 3- and 1 : 2 : 4-trichloro-derivatives were described as monosulphonates.

When the opportunity came for the present authors to complete the sulphonation of the trichloronaphthalenes and examine the derived tetrachloro-derivatives, one of the earliest results was the discovery that, although the salts obtained from the product from the 1 : 2 : 3-derivative were monosulphonates as described (*loc. cit.*), the " chloride $C_{10}H_4Cl_3{\cdot}SO_2Cl$ . . . m. p. 182° " proved to be the disulphonyl chloride $C_{10}H_3Cl_3(SO_2Cl)_2$. Its analysis, numbered CXV, made at the time by the laboratory analyst gave " Cl found 42·79; calc. 43·03%," whereas, with the same specimen, recrystallised to remove surface deterioration, we were unable to obtain a higher value for Cl than 41·26% ($C_{10}H_3O_4Cl_5S_2$ requires Cl, 41·43%). But for that error, it would have been recognised that, under the conditions employed, 1 : 2 : 3-, unlike 1 : 2 : 4-trichloronaphthalene, yields a mixture of mono- and di-sulphonic acids.

Later, it was found that the 1 : 2 : 5-, 1 : 2 : 6-, 1 : 2 : 7-, and 1 : 2 : 8-trichloronaphthalenes under the same conditions also gave mixtures of mono- and di-sulphonic acids. The two products were easy to separate owing to the much greater solubility of the disulphonates in water, but the gelatinous character of their alkali salts and the greater difficulty of converting them into disulphonyl chlorides for identification, led to the replacement of oleum by chlorosulphonic acid, which, when used in molecular proportion, furnished only monosulphonic derivatives.

When it became evident that the sulphonation of 1 : 2 : 3-trichloronaphthalene needed re-examination, the decision was reached to use as source not dichloro-α-naphthol (A. and W., *loc. cit.*) but Widman's tetrachloride obtained by passing chlorine into 1-chloronaphthalene (*Bull. Soc. chim.*, 1878, **28**, 506) and incidentally to ascertain the effect, if any, of solvents on the nature and yield of crystalline additive product. Whereas by the addition of chlorine to 1-chloronaphthalene a 35% yield of crude crystalline product consisting of the tetrachloride, $C_{10}H_7Cl_5$ (m. p. 131°), and 1 : 4-dichloronaphthalene (m. p. 68°) in the approximate proportion of 6 to 1 separated from the accompanying non-crystallisable syrup; and addition in light petroleum (b. p. 100—120°) as solvent gave a similar product but only in one-half the yield; addition in chloroform gave in place of the 1 : 4-dichloronaphthalene a third substance, Widman's 1 : 4-dichloronaphthalene tetrachloride (m. p. 172°), in 22% yield or rather more than thrice the amount of 1-chloronaphthalene tetrachloride isolated. With carbon disulphide as solvent and best in sunlight, a fourth product, the hitherto unknown dichloronaphthalene tetrachloride, m. p. 158°, was encountered, for the preparation of which addition to 1-chloronaphthalene tetrachloride in 10—15 times its weight of disulphide gave the best yields. Hydrogen chloride was emitted in each of these reactions and in the last of them it was accompanied by S_2Cl_2, but whether this played any part in influencing the entry of the substituent chlorine into the second ring could not be ascertained. The viscid material from these sources remained without change over long periods of time: the mixture of tri- and tetrachloronaphthalenes, arising from each by interaction with alkali, proved to be inseparable by either fractional crystallisation or sulphonation.

Whilst 1-chloronaphthalene tetrachloride is homonucleal, Widman's 1 : 4-dichloronaphthalene tetrachloride must be heteronucleal (I), since by decomposition with alkali it yields 1 : 3 : 5 : 8-tetrachloronaphthalene (II). This view is confirmed, inasmuch as by distillation the elimination of 2HCl leads to the production of the 2 : 3 : 5 : 8-isomeride (III):



(II.) (I.) (III.)

No trace of the 1 : 4 : 5 : 8-isomeride, the third possible derivative, was found in either product.

Experimental.

A. *Chloronaphthalene Tetrachlorides.*

(i) *Addition of Chlorine to* 1-*Chloronaphthalene.*—When chlorine was passed into cooled 1-chloronaphthalene (50 g.) rapid absorption took place at first, accompanied by slow evolution of hydrogen chloride. Later, crystals began to form, their separation quickly becoming so abundant as to obstruct the current of gas although less than three-fourths of the calculated amount had been taken up. After being allowed to remain overnight, the product—565 g. from seven operations—was filtered through calico, a tedious process, and the separation (232 g.) spread on porous earthenware. Crystallised from ligroin and later from alcohol, the crude tetrachloride furnished fractions in prismatic forms which fused at 131—132° (133·6 g.); 125—128° (16·3 g.) and 93—121° (7·1 g.), together with flat needles, m. p. 68—69° (23·9 g.), identified as 1 : 4-dichloronaphthalene, and a viscid residue (27·6 g.).

The viscid syrup collected during the original filtration showed no sign of further crystallisation twelve months later. That it likewise contained additive products was evident from its behaviour in alcoholic solution with sodium ethoxide, 21 g. of sodium being required for decomposition of 215 g. of the syrup. After concentration to 300 c.c. and acidification of the alkaline liquor, a crystalline solid (48 g.) and an oil (98 g.) were obtained. The former proved to be a mixture of tri- and tetra-chloronaphthalenes irresolvable into constituents by fractional crystallisation or sulphonation, but from the latter by repeated fractional distillation a separation, m. p. 62—67° (10·9 g.), was isolated from material of lower fusing point and identified as 1 : 4-dichloronaphthalene.

(ii) *Addition of Chlorine to* 1-*Chloronaphthalene dissolved in Light Petroleum* (b. p. 100—120°).—Saturation of a solution of 1-chloronaphthalene (25 g.) in 2 vols. (33 g.) of light petroleum with chlorine (18 g.) gave a well-crystallised product (7·7 g.), easily separated from accompanying viscid material and resolved into 1-chloronaphthalene tetrachloride (5·7 g.) and 1 : 4-dichloronaphthalene (1 g.), m. p. 68°, by fractionation from alcohol. Use of this solvent therefore halved the yield without altering the proportion of the products formed from 1-chloronaphthalene in its absence.

(iii) *Addition of Chlorine to* 1-*Chloronaphthalene in Chloroform Solution.*—When chlorine was passed into 1-chloronaphthalene (32 g.) dissolved in chloroform (80 g.), continuous emission of hydrogen chloride occurred and eventually an abundant crystalline separation which was identified as Widman's 1 : 4-dichloronaphthalene tetrachloride, m. p. 172° (*loc. cit.*), the yield from 192 g. being 80·2 g. and the weight of chlorine absorbed 148 g. (calc. 208 g.).

After removal of as much of the solvent as possible, a highly viscid residue remained which in the course of 2 months became opaque and semi-solid. By filtration, a crystalline magma was collected, which, when dissolved in hot alcohol, furnished separations (41·3 g.) resolved by fractionation into 1-chloronaphthalene tetrachloride, m. p. 117—128° (26·6 g.), and 1 : 4-dichloronaphthalene tetrachloride, m. p. 171—172° (10·9 g.), thus increasing the yield of the latter to 91·1 g. or 22% of that calculated.

As no further separation had taken place in the viscid residue in the course of some months, the greater part (213 g.) was decomposed by alkali, furnishing a solid product (104·5 g.), which after prolonged fractionation was resolved into the following main groups: m. p. 136—145° (58·9 g.); m. p. 95—112° (25·5 g.); m. p. 78—92° (6·9 g.); and m. p. 65—74° (10·3 g.). Of these, the first and the third had respectively the composition of a tetra- and a tri-chloronaphthalene but from neither could a substance of constant m. p. be isolated by the aid of various solvents or by sulphonation.

(iv) *Addition of Chlorine to* 1-*Chloronaphthalene in Carbon Disulphide Solution.*—In the first experiment, saturation of a solution of 1-chloronaphthalene (30 g.) in carbon disulphide (300 g.) with chlorine (35 g.) gave rise to a dark orange liquid from which hydrogen chloride, similarly coloured, slowly escaped during several days, depositing red S_2Cl_2 in small amount in the guard tube. Removal of the solvent in a draught left a syrup which 2 months later had become semicrystalline and, spread on porous earthenware, left a solid (17·2 g.), from which by crystallisation from alcohol a *dichloronaphthalene tetrachloride* (12 g.) was obtained in well-formed, small, elongated prisms, m. p. 158° (Found: Cl, 62·7. $C_{10}H_6Cl_6$ requires Cl, 62·8%).

Repetition of the chlorination thereafter gave disappointing results and in the product one or more of the three—1-chloronaphthalene tetrachloride, 1 : 4-dichloronaphthalene and its tetrachloride—replaced part, and in one case the whole, of the product, m. p. 158°. Especially was this found when the weight of carbon disulphide was reduced to one-fourth and access of light avoided. On the other hand, saturation of the disulphide with chlorine before introduction

of the 1-chloronaphthalene (30 g.)—better still by dissolving 1-chloronaphthalene tetrachloride in the disulphide before passage of the gas—and exposure to bright sunshine until the rapid emission of hydrogen chloride ceased gave yields of 10—13 g., much unchanged (mono)tetrachloride (10—8 g.) being recoverable.

(v) *Conversion of* 1 : 4-*Dichloronaphthalene Tetrachloride, m. p.* 172°, *into* 1 : 3 : 5 : 8-*Tetrachloronaphthalene, m. p.* 131°, *and the derived Pentachloronaphthalene.*—1 : 4-Dichloronaphthalene tetrachloride (60 g.), dissolved in boiling alcohol (3850 c.c.), was decomposed by sodium ethoxide, and the product (46·6 g.) distilled with steam. It crystallised from alcohol in radiate groups of slender needles, m. p. 131° (Found: Cl, 53·2. $C_{10}H_4Cl_4$ requires Cl, 53·4%), and did not depress the m. p. of the tetrachloronaphthalene, m. p. 131°, obtained from 1 : 3 : 8-trichloronaphthalenesulphonyl chloride, m. p. 127° (see p. 254). It is therefore the 1 : 3 : 5 : 8-derivative.

1 : 3 : 5 : 8-*Tetrachloronaphthalenesulphonic Acid.*—When this tetrachloronaphthalene (30 g.), dissolved in carbon disulphide, was shaken vigorously with chlorosulphonic acid (16 g.) under the conditions described on p. 247, very little emission of hydrogen chloride was observed; 15·5 g. of the substance were recovered unchanged; and the sulphonic acid on neutralisation furnished 19·7 g. of the oven-dried sodium salt. By doubling the amount of chlorosulphonic acid the weight of substance recovered (11·4 g.) showed a reduction of only 25% : this however was not wholly unchanged material, m. p. 131°, but contained about one-fourth its weight of an unidentified fraction of higher m. p. 162—172°. Sulphonation with 8 times the weight (50% excess) of 5% oleum at 100° produced much darkening but gave as sole product in poor yield a sodium salt identical with that obtained by the use of chlorosulphonic acid.

The *sodium* salt crystallised in sparingly soluble needles (Found: Na, 5·9; H_2O, 5·0. $C_{10}H_3O_3Cl_4SNa,H_2O$ requires Na, 6·0; H_2O, 4·7%) and the *sulphonyl chloride* from benzene in small prismatic forms, m. p. 146° (Found: Cl, 48·7. $C_{10}H_3O_2Cl_5S$ requires Cl, 48·7%). Heated with phosphorus pentachloride (30 g.) at 198—215° during 2 hours, the chloride (24·6 g.) gave crude *pentachloronaphthalene* (16·5 g.), which after distillation with steam crystallised from alcohol in moderately soluble, long, slender needles, m. p. 155° (Found: Cl, 58·7. $C_{10}H_3Cl_5$ requires Cl, 59·1%).

(vi) *Conversion of* 1 : 4-*Dichloronaphthalene Tetrachloride, m. p.* 172°, *into* 1 : 4 : 6 : 7(2 : 3 : 5 : 8-)-*Tetrachloronaphthalene and the derived Pentachloronaphthalene.*—Alternatively, when this tetrachloride (40 g.) was heated at 330—356°, it gave together with a continuous emission of hydrogen chloride a yellow distillate (29 g.), which solidified on cooling and when crystallised from alcohol formed long, flexible, yellow needles (26·3 g.), m. p. 133—136°, later identified as the 2 : 3 : 5 : 8-*tetrachloronaphthalene* (Found: Cl, 53·2. $C_{10}H_4Cl_4$ requires Cl, 53·4%).

2 : 3 : 5 : 8-*Tetrachloronaphthalenesulphonic Acid.*—As sulphonation with 1 mol. prop. of chlorosulphonic acid left much of the 2 : 3 : 5 : 8-tetrachloronaphthalene (16 g.) unchanged, twice the weight (16 g.) was added to the solution in carbon disulphide and the whole shaken continuously until the product solidified. Nevertheless, one-fourth (4·3 g.) of the substance was recovered, of which, when recrystallised, 3·4 g. had the m. p. 133—134°. From the solution, the sodium salt could only be separated in gelatinous form: it was therefore converted into the *sulphonyl chloride*, which dissolved easily in benzene and on admixture with much petrol gave small, radiate, flat needles, m. p. 133° (Found: Cl, 48·5. $C_{10}H_3O_2Cl_5S$ requires Cl, 48·7%). Regenerated from the chloride, the *sodium* salt, moderately soluble in water, separated at first as a jelly-like suspension of needles which, left for a few days in the solvent, underwent transformation into glistening, flat needles (Found: Na, 5·9; H_2O, 4·4. $C_{10}H_3O_3Cl_4SNa,H_2O$ requires Na, 6·0; H_2O, 4·7%).

Hydrolysis of the sodium salt (6·3 g.), suspended in orthophosphoric acid (*d* 1·75), with steam at 240—250° regenerated the tetrachloronaphthalene (3·1 g.), which crystallised from alcohol in slender, long needles but, left in the solution, changed into flat, elongated prisms and had two m. p.'s, 139° and 133°. The former was usually observed, but if the fused substance was allowed to cool in the bath until solidification occurred and the temperature at once raised, the translucent mass had the lower m. p.; whereas if a short time elapsed before heating was resumed it became suddenly opaque and then melted at 139°. By this behaviour, the tetrachloronaphthalene was identified with the product obtained from 2 : 3 : 5-trichloronaphthalenesulphonyl chloride (p. 256), the m. p.'s of which it did not depress, and is therefore the 2 : 3 : 5 : 8-derivative.

Heated with phosphorus pentachloride (16 g.) at 180—190° during 2 hours, the sulphonyl chloride (7·8 g.) gave a *pentachloronaphthalene* (4·3 g.), which crystallised from light petroleum (b. p. 80—100°) in small, soft, opaque balls composed of microscopic needles, m. p. 131°, and

on cooling in the bath became translucent at 108°, clear at 110°, but opaque if kept for a few seconds and then did not fuse below 131° (Found : Cl, 59·3. $C_{10}H_3Cl_5$ requires Cl, 59·1%).

(vii) *Conversion of Dichloronaphthalene Tetrachloride, m. p. 157°, into Tetrachloronaphthalene and the derived Pentachloronaphthalene.*—When the tetrachloride, m. p. 157°, (30 g.) in alcoholic solution was decomposed by sodium ethoxide, it gave a *tetrachloronaphthalene* (22·8 g.), which distilled with steam with unusual slowness and when dry was most troublesome to wet with water. By fractionation from alcohol, it was found to be uniform and to crystallise in lustrous, slender, flat needles, m. p. 196° (Found : Cl, 53·3. $C_{10}H_4Cl_4$ requires Cl, 53·4%).

Tetrachloronaphthalenesulphonic Acid.—Chlorosulphonic acid being ineffective, the tetrachloronaphthalene (17·8 g.) was heated with 8 times its weight of 5% oleum at 150° until in the course of an hour sulphonation was complete. The dark-coloured product, poured on ice, gave much gelatinous material, which, dissolved in hot water, was neutralised with baryta and converted into sodium salt, and the solution, owing to its gelatinous character, evaporated to dryness. The dry residue (20·5 g.), converted into *sulphonyl chloride*, furnished two products, of which the less soluble major constituent crystallised from light petroleum (b. p. 100—120°) in glistening scales or thin prisms, m. p. 132°, but from benzene in fairly large prisms which when freshly removed from the solution had no sharp m. p. (107—122°) owing to loss of " benzene of crystallisation " [Found : C_6H_6, 9·7. $(C_{10}H_3O_2Cl_5S)_2,C_6H_6$ requires C_6H_6, 9·7%]. On removal of the benzene, the crystals became opaque and had m. p. 132° (Found : Cl, 48·6. $C_{10}H_3O_2Cl_5S$ requires Cl, 48·7%), but when the fused substance was cooled rapidly in the air or slowly in the bath it solidified as a translucent mass, m. p. 122—123°. If seeded on refusion or just before solidification with a crystal having the higher m. p., the less fusible form separated in scales, m. p. 132°. On hydrolysis, the chloride gave the sparingly soluble *sodium tetrachloronaphthalenesulphonate*, which crystallised in microscopic needles grouped together in opaque scales or semi-gelatinous flocks (Found : Na, 5·8; H_2O, 4·4. $C_{10}H_3O_3Cl_4SNa,H_2O$ requires Na, 6·0; H_2O, 4·7%). When heated with phosphorus pentachloride (8 g.) at 192—208° during 2 hours, the chloride (6·8 g.) gave the corresponding *pentachloronaphthalene* (3·0 g.), which crystallised from alcohol in sparingly soluble, very slender needles, m. p. 147° (Found : Cl, 58·7. $C_{10}H_3Cl_5$ requires Cl, 59·1%).

The minor constituent, m. p. 199—200°, isolated in small amount from the sulphonyl chloride preparation, was not further examined.

B. *Sulphonation of the Trichloronaphthalenes.*

The sulphonation of these compounds was carried out in 5—6 times the weight of carbon disulphide, a small excess of chlorosulphonic acid beyond 1 mol. being added drop by drop with continuous shaking until either the product solidified or the emission of hydrogen chloride became negligible. After removal of the solvent by distillation on a water-bath, the solution of the sulphonic acid in water was distilled with steam to remove unchanged trichloronaphthalene, usually small in amount; filtered to collect insoluble material, chiefly sulphone; and converted successively into the barium and sodium salts, which in turn were fractionally crystallised. From the sodium salt, the sulphonyl chloride and finally the tetrachloronaphthalene were obtained by interaction with phosphorus pentachloride. The latter product invariably contained unchanged chloride which, after hydrolysis in alcoholic solution with sodium ethoxide, was removed by extraction with water. Introduction of some small amount of impurity arising from the chlorinating action of the pentachloride at the temperature, *ca.* 180—210°, employed could not be avoided and for its removal, being the less volatile, distillation with steam, unless too slow, rather than fractional crystallisation was the more effective.

Trichloronaphthalene.	Sulphonyl chloride, m. p.	Tetrachloronaphthalene. M. p.	Tetrachloronaphthalene. Constitution.
1 : 2 : 3	131° and 157°	144°	1 : 2 : 3 : 5
		115	1 : 2 : 3 : 7
1 : 2 : 4	158	111	1 : 2 : 4 : 6
1 : 2 : 5	146 and 179	164	1 : 2 : 5 : (?)
		110, 114	1 : 2 : 5 : (?)
1 : 2 : 6	184	111	1 : 2 : 4 : 6
1 : 2 : 7	176	144	1 : 2 : 7 : (?)
1 : 2 : 8	105	135	1 : 2 : 8 : (?)
1 : 3 : 5	152	179	1 : 3 : 5 : 7
1 : 3 : 6	156	119	1 : 3 : 6 : 7
1 : 3 : 7	138	179	1 : 3 : 5 : 7
1 : 3 : 8	127	131	1 : 3 : 5 : 8
1 : 4 : 7	144	109	1 : 4 : 7 : (?)

Trichloronaphthalene.	Sulphonyl chloride, m. p.	Tetrachloronaphthalene. M. p.	Tetrachloronaphthalene. Constitution.
1 : 4 : 8	118° and 178°	131°	1 : 3 : 5 : 8
		144	1 : 4 : 8 : (?)
2 : 3 : 5	164	134, 139	2 : 3 : 5 : 8
2 : 3 : 6	94 and 118	218	3 : 6 : 7 : (?)
		120	1 : 3 : 6 : 7

Dichloronaphthalene tetrachloride.	Tetrachloronaphthalene. M. p.	Tetrachloronaphthalene. Constitution.
1 : 4-Cl_2,Cl_4 (m. p. 172°)	131° and 133, 139	1 : 3 : 5 : 8
		2 : 3 : 5 : 8
Cl_2,Cl_4 (m. p. 157°)	196	1 : (?) : (?) : (?)

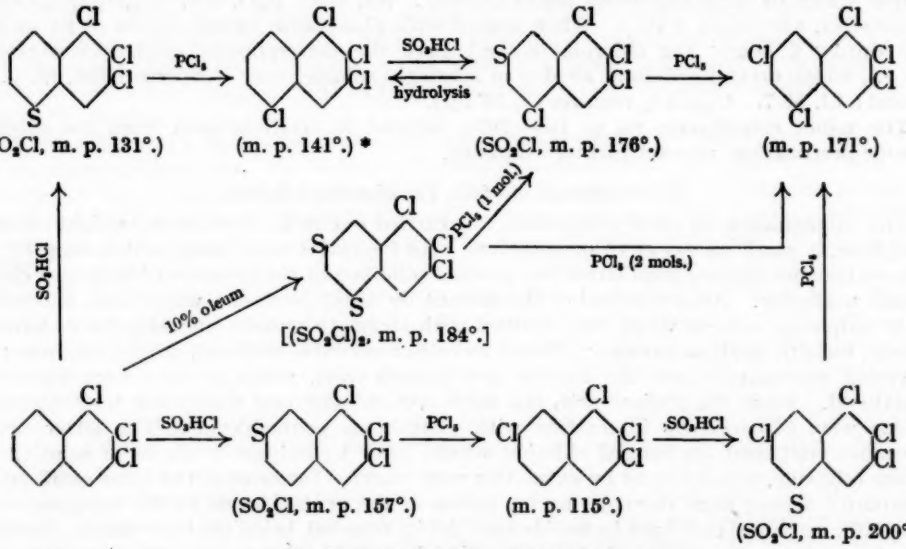
In the table are given the m. p.'s of the sulphonyl chlorides and tetrachloronaphthalenes obtained from the trichloronaphthalenesulphonic acids and of three tetrachloronaphthalenes obtained from two dichloronaphthalene tetrachlorides. The six tetrachloronaphthalenes hitherto prepared are of unknown constitution. One of them, that known as δ, m. p. 141°, is probably included among the fifteen now described (seven short of the possible number on the basis of the Erlenmeyer symbol) and with one exception the relative position of at least three chlorine atoms is known in each.

Only with 1 : 2 : 3-trichloronaphthalene has the study of sulphonation products been extended to include the pentachloro-derivative. The outcome shown in the diagram is based on conclusions which, lacking an independent check, depend on the following considerations:

(i) Substitution in the naphthalene series takes place preferentially in an α- and, if simultaneously, only to a subsidiary extent in a β-position.

(ii) Replacement of SO_2Cl by Cl when a sulphonyl chloride is heated either with phosphorus pentachloride, or more slowly alone, takes place more readily (*e.g.*, at a lower temperature) in an α- than in a β-position.

(iii) The chief product of the sulphonation of the 1 : 2-, 1 : 3-, and 2 : 3-dichloronaphthalenes is the 5-derivative (A. and W., Proc. 1890, 78, 79); it is reasonable therefore to conclude that this will also be the 5-acid when 1 : 2 : 3-trichloronaphthalene is sulphonated by the same agent, SO_3HCl, under similar conditions. Granted that the preferential or α-position for mono-sulphonation is 5, it follows that the position assumed in disulphonation must be 7- for the reason that the 4-, 6-, and 8-positions are inhibited by "the 'invincible objection' of two sulphonic groups to remain in either contiguous, or para- or peri-positions relatively to one another when disulphonic acids are formed by the action of sulphuric acid on naphthalene or on the chloro-, amido-, or hydroxy-naphthalenes" (A. and W., *ibid.*, 1893, 166) (S = SO_3H).



I. 1 : 2 : 3-*Trichloronaphthalene.*

1 : 2 : 3-Trichloronaphthalene (61 g.) was obtained when 1-chloronaphthalene tetrachloride (126 g.), dissolved in boiling alcohol, was decomposed with alcoholic sodium ethoxide (sodium, 19 g.). It crystallised at first in long, slender needles, which changed over-night in the solution into clusters of short rods, semi-opaque when dry, m. p. 80·5°. The by-products (30·5 g.) fused at temperatures ranging over the interval 69—112°.

The crucial test for freedom from impurity was the behaviour of the substance in a m. p. tube. If the fused specimen was allowed to cool in the bath to 68° and then withdrawn, it solidified immediately to a translucent mass which on swift re-immersion had the m. p. 66—67°, but if left in the air for a few seconds became opaque suddenly, forming a cylinder, m. p. 82—

* On the assumption that Atterberg and Widman's 1 : 5-dichloronaphthalene tetrachloride loses 2HCl in the same way as 1-chloronaphthalene tetrachloride, it follows that the tetrachloronaphthalene, m. p. 141°, obtained by them is likewise the 1 : 2 : 3 : 5-derivative.

83°, retracted from the wall of the capillary tube. The transformation, although slower, also occurred in the translucent substance if retained in the bath below 66°. Fractions which did not suffer this change were rejected as impure even although their m. p.'s were in the neighbourhood of 80—81°.

When the sulphonation of 1 : 2 : 3-trichloronaphthalene was taken up afresh with the object of preparing the sulphonyl chloride for conversion into the tetrachloro-derivative, 10% oleum as in 1890 being the agent used (A. and W., *loc. cit.*, p. 76), the sulphonyl chloride prepared from the potassium monosulphonate had unexpectedly the m. p. 131°, not 182° as previously recorded and yet was a monosulphonyl derivative (Found : Cl, 42·8. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%). As the authors' analysis showed the original specimen to be a disulphonyl chloride (see p. 244), evidence for the presence of disulphonate was sought in the mother-liquors of the potassium monosulphonate. These by fractional crystallisation furnished scales of the very soluble salt, $C_{10}H_3Cl_3(SO_3K)_2,3H_2O$, in small amount, the chloride from which melted at 184° and did not depress the m. p. of the supposed " monosulphonyl " derivative.

Incidentally, on the addition of ligroin to the benzene solution from which the chloride, m. p. 131°, had been mostly removed, a second product separated in needles, m. p. *ca.* 117—120°, which had a similar composition (Found : Cl, 42·7%). Thereafter, chlorosulphonic acid, which furnished only monosulphonyl derivatives, replaced oleum (see p. 244) and the separation of the derived sulphonyl chloride into its proximate constituents was effected by adding to its solution in benzene sufficient petrol to eliminate the least soluble fraction as needles, m. p. *ca.* 117—120°, and then removing the petrol by distillation to ensure separation of the chloride, m. p. 131°, from benzene. A third constituent in small amount, forming prisms, m. p. *ca.* 157°, was separated by hand from the clustered needles of the final crystallisations of this fraction, m. p. 131°. As a first approximation, the yield from 160 g. of 1 : 2 : 3-trichloronaphthalene amounted to 18·5 g., m. p. 99—106°; 54·6 g., m. p. 117—121°; 99·0 g., m. p. 123—131°; 8·1 g., m. p. 135—149°. But whilst the chlorides, m. p. 131° and 157°, were undoubted isomerides, the third, m. p. *ca.* 119°, proved to be a mixture of these which survived attempts to effect a separation by the aid of solvents of various types but, on hydrolysis in alcoholic solution with sodium ethoxide and conversion into barium salt, yielded to systematic fractionation, followed by regeneration of chloride from the isomeric sulphonates. In the most fruitful of these hydrolyses, 24·3 g., m. p. 117—119°, gave as product 7·7 g., m. p. 118—119°; 6·6 g., m. p. 129—131°; and 2·7 g., m. p. 156—157°; together with small fractions below 116° and above 121°. As determined by the Taupunkt method (Davies, J., 1921, **119**, 862), the fraction, m. p. 118—119°, contained 37% of the chloride, m. p. 157°.

1 : 2 : 3-*Trichloronaphthalenesulphonic Acid* (chloride, m. p. 131°).—The barium and potassium salts have been described (Proc., *loc. cit.*). The *sodium* salt crystallised in comparatively sparingly soluble, nacreous scales (Found : Na, 6·2; H_2O, 5·2. $C_{10}H_4O_3Cl_3SNa,H_2O$ requires Na, 6·5; H_2O, 5·1%), and the *amide* from alcohol in very sparingly soluble needles, m. p. 249° (Found : N, 4·4. $C_{10}H_6O_2NCl_3S$ requires N, 4·5%).

When heated with an equal weight of phosphorus pentachloride at 178—181° during 2·5 hours, the sulphonyl chloride, m. p. 131°, was converted almost quantitatively into 1 : 2 : 3 : 5-*tetrachloronaphthalene* (for constitution, see p. 248), which crystallised from alcohol in somewhat sparingly soluble needles, m. p. 141° (Found : Cl, 53·1. $C_{10}H_4Cl_4$ requires Cl, 53·4%).

1 : 2 : 3 : 5-*Tetrachloronaphthalenesulphonic Acid.*—On sulphonation in carbon disulphide solution with chlorosulphonic acid (12 g.), the tetrachloro-derivative (24 g.) was rapidly converted into a crystalline product which, after dissolution in water and neutralisation with sodium hydroxide, gave 29 g. of sulphonate, the amount of unchanged substance and of " sulphone " being 0·9 g. and 1·9 g. respectively. The corresponding sulphonyl chloride (19·7 g.) crystallised from benzene or from light petroleum (b. p. 100—120°) in minute scales, m. p. 176°, and by a mixed m. p. determination proved to be identical with the monosulphonyl chloride, m. p. 176°, obtained from 1 : 2 : 3-trichloronaphthalenedisulphonyl chloride, m. p. 184°, as subsidiary product when heated with phosphorus pentachloride. The *sodium* salt, regenerated from the chloride, crystallised in moderately soluble, hair-like forms grouped together in clots (Found : Na, 5·8; H_2O, 7·3. $C_{10}H_3O_3Cl_4SNa,1·5H_2O$ requires Na, 5·8; H_2O, 6·8%).

From the chloride (10·5 g.), when heated with phosphorus pentachloride (15 g.) at 203—210° during 3 hours, a product was obtained which proved to be 1 : 2 : 3 : 5 : 7-*pentachloronaphthalene* and crystallised from 1650 c.c. of boiling alcohol in long needles (5·5 g.), m. p. 171° (Found : Cl, 58·8. $C_{10}H_3Cl_5$ requires Cl, 59·1%).

From the final mother-liquors of the chloride in light petroleum, a second product, m. p. 132—134°, was isolated, but in amount too small for its identity to be established.

1 : 2 : 3-*Trichloronaphthalenesulphonic Acid* (chloride, m. p. 157°).—The *sodium* salt, regenerated from the chloride, formed comparatively sparingly soluble, lustrous scales (Found: Na, 6·5; H_2O, 4·5. $C_{10}H_4O_3Cl_3SNa,H_2O$ requires Na, 6·5; H_2O, 5·1%). The *amide* crystallised from alcohol in moderately soluble, well-defined needles, m. p. 245° (Found: N, 4·5. $C_{10}H_6O_2NCl_3S$ requires N, 4·5%). On hydrolysis with superheated steam, the salt furnished 1 : 2 : 3-trichloronaphthalene, m. p. 84°, confirmed by the lower m. p. 68° and opacity at 64·5° (see p. 248).

When the sulphonyl chloride (9·2 g.) was heated with phosphorus pentachloride (7·5 g.) at 187—192° during 2 hours, and the product distilled with steam, 1 : 2 : 3 : 7-*tetrachloronaphthalene* (4·6 g.) was obtained, which crystallised from alcohol in soft, flat, slender needles, m. p. 115° (Found: Cl, 53·4. $C_{10}H_4Cl_4$ requires Cl, 53·4%).

1 : 2 : 3 : 7-*Tetrachloronaphthalenesulphonic Acid*.—On sulphonation with chlorosulphonic acid (4·1 g.), the tetrachloro-derivative, m. p. 115° (7·2 g.) gave a product from which a small amount of unchanged tetrachloronaphthalene (1·6 g.) was recovered. The sparingly soluble *sodium* salt crystallised in very small scales (Found: Na, 5·8; H_2O, 8·5. $C_{10}H_3O_3Cl_4SNa,2H_2O$ requires Na, 5·7; H_2O, 8·9%). Later separations were mixtures of small scales with flocculent forms, the latter being removed by warming carefully the suspension in its mother-liquor, it being the more soluble. Eventually the whole of the salt (7·1 g.) was obtained in three fractions, which on conversion into sulphonyl chloride and fractional crystallisation first from benzene and later with the addition of petrol to the mother-liquors gave two products, the larger (4·2 g.), m. p. 199°, and the smaller (0·4 g.), m. p. 154—155°. The former, sparingly soluble in benzene, crystallised in small prisms (Found: Cl, 48·3. $C_{10}H_3O_2Cl_5S$ requires Cl, 48·7%). For conversion into *pentachloronaphthalene*, 3·5 g. were heated with phosphorus pentachloride (6 g.) at 213—220° during 1·5 hours. The product (2·8 g.) on distillation with steam gave only 0·49 g. in 28 hours. This small amount required no less than 150 c.c. of boiling alcohol for solution, crystallising therefrom in stellate groups of short, slender needles, m. p. 171° (Found: Cl, 59·1. $C_{10}H_3Cl_5$ requires Cl, 59·1%), and is identical with the 1 : 2 : 3 : 5 : 7-pentachloronaphthalene obtained from trichloronaphthalenedisulphonyl chloride (m. p. 184°) (see below) and tetrachloronaphthalenesulphonyl chloride (m. p. 176°) (see p. 249).

The amount (0·4 g.) of the substance, m. p. 154—155°, was too small to admit of the determination of its relationships.

1 : 2 : 3-*Trichloronaphthalenedisulphonic Acid*.—When 1 : 2 : 3-trichloronaphthalene (30 g.) was shaken continuously with 10% oleum (200 g.) at 100°, the clear solution first formed became a thick dark mass of crystalline product in the course of 15 minutes. Dissolved in water and neutralised by baryta, the product gave a bulky precipitate, from which the highly soluble sulphonate was removed by repeated extraction with boiling water, but did not separate from solution until the volume (30 l.) was reduced to less than 500 c.c. The *barium* salt was ill defined and granular (Found: Ba, 22·4; H_2O, 13·1. $C_{10}H_3O_6Cl_3S_2Ba,4H_2O$ requires Ba, 22·9; H_2O, 12·0%); the *potassium* salt crystallised in easily soluble, small, lustrous scales (Found: K, 15·0; H_2O, 10·2. $C_{10}H_3O_6Cl_3S_2K_2,3H_2O$ requires K, 15·0; H_2O, 10·3%); and the *disulphonyl chloride* from benzene in small prisms or fan-like, slender prismatic aggregates, m. p. 184° (Found: Cl, 41·1. $C_{10}H_3O_4Cl_5S_2$ requires Cl, 41·4%).

When heated with an equal weight of phosphorus pentachloride at 183—188° during 2·5 hours, the disulphonyl chloride (40 g.) was converted into a mixture of two products, which were separated by digesting it in alcoholic solution with potassium hydroxide (12 g.), removing the alcohol by distillation, and extracting the dry residue with boiling water.

(i) The substance insoluble in water proved to be 1 : 2 : 3 : 5 : 7-*pentachloronaphthalene* (10 g.), which crystallised from alcohol in very sparingly soluble, slender needles showing pronounced "electrical" properties when dry, m. p. 171° (Found: Cl, 59·2. $C_{10}H_3Cl_5$ requires Cl, 59·1%).

(ii) The substance soluble in water was *potassium tetrachloronaphthalenesulphonate* (10·2 g.), which, being sparingly soluble, was easily separated from unchanged trichloronaphthalenedisulphonate; it crystallised in tufts of slender needles (Found: K, 9·5; H_2O, 4·0. $C_{10}H_3O_3Cl_4SK,H_2O$ requires K, 9·7; H_2O, 4·5%). Only by using the lowest temperature possible was the yield of this intermediate product of the interaction at all considerable. The *barium* salt, soluble only to the extent of 1·0 g. in 15 l. of boiling water, crystallised in a felt of hair-like needles (Found: Ba, 15·5; H_2O, 6·4. $C_{20}H_6O_6Cl_8S_2Ba,3H_2O$ requires Ba, 15·6; H_2O, 6·1%); the *sulphonyl chloride* from benzene in radiate groups of needles, m. p. 176° (Found: Cl, 48·9. $C_{10}H_3O_3Cl_5S$ requires Cl, 48·7%); and the *amide* from alcohol in moderately soluble, fan-like groups of needles, nacreous when dry, m. p. 235° (Found: N, 4·0. $C_{10}H_5O_2NCl_4S$ requires N, 4·1%).

By interaction with phosphorus pentachloride, the sulphonyl chloride was converted into the 1 : 2 : 3 : 5 : 7-pentachloronaphthalene, m. p. 171°, and, by hydrolysis in orthophosphoric acid suspension with superheated steam, the potassium salt into 1 : 2 : 3 : 5-tetrachloronaphthalene, m. p. 141°, identical with the product obtainable from 1 : 2 : 3-trichloronaphthalenesulphonyl chloride, m. p. 131° (see p. 249).

II. 1 : 2 : 4-*Trichloronaphthalene.*

This trichloronaphthalene was obtained from 2 : 4-dichloro-1-aminonaphthalene; it melted at 92°. On sulphonation (60 g.) with chlorosulphonic acid (43 g.) a product was obtained from which unchanged trichloronaphthalene (0·9 g.) was recovered and non-volatile residue (11·0 g.) collected. The barium and potassium salts have been described (A. and W., Proc., *loc. cit.*); the *sulphonyl chloride* obtained from the latter crystallised for the most part in needles easily soluble in benzene but only sparingly so in ligroin, m. p. 158° (Found : Cl, 42·6. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%), whilst from the mother-liquors a possible isomeride separated in small, opaque spherules (3·6 g.), the purest form of which had m. p. 124—129° (Found : Cl, 41·7%) and was not further examined. Heated with an equal weight of phosphorus pentachloride at 185—198° during 3 hours, the chloride yielded a *tetrachloronaphthalene* which crystallised from alcohol in radiate groups of slender needles, m. p. 111° (Found : Cl, 53·3. $C_{10}H_4Cl_4$ requires Cl, 53·4%), and was identified by a mixed m. p. determination with the tetrachloro-derivative obtained from 1 : 2 : 6-trichloronaphthalenesulphonyl chloride (p. 252).

Sulphonation of this tetrachloro-derivative had to be effected by 10% oleum, since in carbon disulphide solution it was only slightly attacked by chlorosulphonic acid. Introduced into 3·5 times its weight of oleum and heated at 150° for an hour, it furnished a *sodium* salt by the usual method, which crystallised in easily soluble, minute scales or in feathery forms (Found : Na, 5·9; H_2O, 6·8. $C_{10}H_3O_3Cl_4SNa,1·5H_2O$ requires Na, 5·8; H_2O, 6·8%). On hydrolysis with superheated steam, this salt, suspended in orthophosphoric acid at 280°, gave a 45% yield of the tetrachloronaphthalene, m. p. 111°. The *sulphonyl chloride* crystallised from benzene in readily soluble, hemispherical aggregates of prismatic needles, m. p. 140° (Found : Cl, 48·0. $C_{10}H_3O_2Cl_5S$ requires Cl, 48·7%), and when heated (13·5 g.) with phosphorus pentachloride (20 g.) at 190—202° during 3 hours gave the 1 : 2 : 4 : 6 : (?)-*pentachloronaphthalene* (5·5 g.), which crystallised from alcohol in sparingly soluble clusters of very slender needles, opaque and " electrical " when dry, m. p. 135° (Found : Cl, 59·0. $C_{10}H_3Cl_5$ requires Cl, 59·1%).

III. 1 : 2 : 5-*Trichloronaphthalene.*

The 1 : 2 : 5-trichloronaphthalene was obtained from 1-chloro-2-aminonaphthalene-5-sulphonic acid (" No. 1 acid "; cf. A. and W., Proc., 1889, 36, 49) and purified by distillation with steam. It fused at 79°, but if allowed to cool slowly in the bath or rapidly in the air, solidified at 69° to a translucent, crystalline mass which, when the temperature was immediately raised, fused at 74° but when allowed to remain at or below 69° for a few minutes became opaque and, as at first, fused at 79°.

After sulphonation of this derivative (30 g.) with chlorosulphonic acid (20 g.) and recovery of unchanged trichloronaphthalene (5·9 g.), followed by collection of non-volatile, insoluble matter (2·7 g.), the product on conversion into the potassium salt was found to consist of two isomerides, of which the less soluble was isolated without difficulty. From the concentrated aqueous mother-liquors, separations were obtained which after conversion into sulphonyl chloride and fractional crystallisation from benzene furnished on hydrolysis the readily soluble salt of the isomeride. Finally, from the concentrated benzene mother-liquors, after addition of ligroin, a separation in small, opaque, spherical particles, m. p. 120—126°, was obtained (Found : Cl, 42·8%), amounting to some 10% of the original sulphonation product, which, although inseparable by fractional crystallisation, proved on conversion into alkali salt to be not a third isomeride but a mixture of the two already isolated. The acid forming the less soluble salts constituted approximately 70% of the product.

The less soluble, anhydrous *potassium* salt crystallised in glistening, slender, elongated scales (Found : K, 11·1. $C_{10}H_4O_3Cl_3SK$ requires K, 11·2%); the *sodium* salt in small nacreous scales (Found : Na, 6·6; H_2O, 5·3. $C_{10}H_4O_3Cl_3SNa,H_2O$ requires Na, 6·5; H_2O, 5·1%); and the *sulphonyl chloride* from benzene in small well-formed prisms, m. p. 146° (Found : Cl, 43·0. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%). Heated with phosphorus pentachloride (30 g.) at 185—195° during 3 hours, the chloride (18 g.) was converted into a 1 : 2 : 5 : (?)-*tetrachloronaphthalene* (13·6 g.), which crystallised in sparingly soluble, soft, feathery needles, m. p. 164° (Found : Cl, 53·4. $C_{10}H_4Cl_4$ requires Cl, 53·4%).

The more soluble *potassium* salt separated in flocculent groups of minute hair-like forms (Found: K, 10·9; H_2O, 4·7. $C_{10}H_4O_3Cl_3SK,H_2O$ requires K, 10·6; H_2O, 4·9%); the *sodium* salt in small, ill-defined forms (Found: Na, 6·4; H_2O, 7·2. $C_{10}H_4O_3Cl_3SNa,1·5H_2O$ requires Na, 6·4; H_2O, 7·5%); and the *sulphonyl chloride* from benzene in easily soluble, narrow, elongated prisms, m. p. 179° (Found: Cl, 42·8. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%). Heated with phosphorus pentachloride (9 g.) at 195—198° during 2·75 hours, the chloride (5·5 g.) was converted into a 1 : 2 : 5 : (?)-*tetrachloronaphthalene* (3·1 g.), which crystallised from alcohol in radiate groups of slender needles (Found: Cl, 53·3. $C_{10}H_4Cl_4$ requires Cl, 53·4%). It had the m. p. 114° when first fused but repeatedly, after solidifying to a translucent mass at *ca.* 98°, was found to melt at 110° except for a few crystalline particles which in favourable circumstances acted as nuclei for the form of higher m. p. provided the bath was allowed to cool slowly.

IV. 1 : 2 : 6-*Trichloronaphthalene.*

The 1 : 2 : 6-trichloronaphthalene used was obtained from 1-chloro-2-aminonaphthalene-6-sulphonic acid ("No. 2 acid"; A. and W., *loc. cit.*), and had m. p. 92°. When sulphonated with chlorosulphonic acid (13 g.), this 1 : 2 : 6-trichloronaphthalene (20 g.) gave a solid product from which unchanged trichloro-derivative (0·2 g.) was recovered and non-volatile, insoluble material (6·7 g.) collected. The *sodium* salt crystallised in easily soluble, feathery needles (Found: Na, 6·2; H_2O, 9·6. $C_{10}H_4O_3Cl_3SNa,2H_2O$ requires Na, 6·2; H_2O, 9·7%), and the *sulphonyl chloride* from benzene in easily soluble, flat prisms, m. p. 184° (Found: Cl, 43·3. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%). Heated with twice its weight of phosphorus pentachloride at 195—202° during 3 hours, the chloride was converted into a *tetrachloronaphthalene*, which crystallised from alcohol in long, slender needles, m. p. 111° (Found: Cl, 53·4. $C_{10}H_4Cl_4$ requires Cl, 53·4%). It did not depress the m. p. of the tetrachloronaphthalene, m. p. 111°, obtained from 1 : 2 : 4-trichloronaphthalenesulphonyl chloride, m. p. 158° (p. 251), whence it follows that each is the 1 : 2 : 4 : 6-derivative.

V. 1 : 2 : 7-*Trichloronaphthalene.*

The 1 : 2 : 7-trichloronaphthalene, m. p. 88° (also 84°), used for sulphonation was obtained from 1-chloro-2-aminonaphthalene-7-sulphonic acid ("No. 3 acid"; A. and W., *loc. cit.*). When sulphonated by half its weight of chlorosulphonic acid, it gave a product free from unchanged trichloronaphthalene, the amount of non-volatile, insoluble substance being negligible. The *barium* salt crystallised in radiating clusters of needles (Found: Ba, 16·8; H_2O, 7·9. $C_{20}H_8O_6Cl_6S_2Ba,3·5H_2O$ requires Ba, 16·7; H_2O, 7·7%); the *potassium* salt in long, thin laminæ (Found: K, 10·5; H_2O, 4·9. $C_{10}H_4O_3Cl_3SK,H_2O$ requires K, 10·6; H_2O, 4·9%); the *sodium* salt in sparingly soluble, long, flat needles (Found: Na, 6·6; H_2O, 5·1. $C_{10}H_4O_3Cl_3SNa,H_2O$ requires Na, 6·5; H_2O, 5·1%); and the *sulphonyl chloride* from benzene in small prisms, m. p. 176° (Found: Cl, 42·7. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%). From the chloride, when heated with an equal weight of phosphorus pentachloride at 185—195° during 2 hours, 1 : 2 : 7 : (?)-*tetrachloronaphthalene* was obtained in good yield: it crystallised from alcohol in small groups of needles, m. p. 144° (Found: Cl, 53·4. $C_{10}H_4Cl_4$ requires Cl, 53·4%).

VI. 1 : 2 : 8-*Trichloronaphthalene.*

The 1 : 2 : 8-trichloronaphthalene, m. p. 84°, employed was obtained from 1 : 2-dichloronaphthalene-8-sulphonyl chloride, m. p. 138°, itself prepared from the amino-derivative formed from Cleve's 2-chloro-1-nitronaphthalene-8-sulphonyl chloride. When sulphonated with two-thirds its weight of chlorosulphonic acid, the product solidified to a mass of small particles soon after addition was complete. From the solution of the acid in water the trichloronaphthalene recovered and insoluble, non-volatile residue collected were negligible in amount. The *barium* salt crystallised in sparingly soluble, fern-like groups of short needles (Found: Ba, 17·8; H_2O, 2·8. $C_{20}H_8O_6Cl_6S_2Ba,H_2O$ requires Ba, 17·7; H_2O, 2·3%); the *potassium* salt in readily soluble, anhydrous, diamond-shaped, lustrous plates (Found: K, 11·1. $C_{10}H_4O_3Cl_3SK$ requires K, 11·2%); and the *sulphonyl chloride* in well-developed, elongated prisms, easily soluble in benzene but only sparingly so in petrol, m. p. 105° (Found: Cl, 42·7. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%). No evidence of the presence of an isomeride was discovered; the trichloronaphthalene regenerated by hydrolysis of the sodium salt with superheated steam had m. p. 84°. Heated with phosphorus pentachloride (21 g.) at 188—205° during 2·5 hours, the chloride (15 g.) was converted into 1 : 2 : 8 : (?)-*tetrachloronaphthalene* (11·4 g.), which crystallised from alcohol in moderately soluble, slender needles, m. p. 135°, and was only very slightly volatile with steam, not more than 1 g. passing over in 70 hours (Found: Cl, 54·3. $C_{10}H_4Cl_4$ requires Cl, 53·4%).

VII. 1 : 3 : 5 (2 : 4 : 8)-*Trichloronaphthalene.*

1 : 3 : 5-Trichloronaphthalene, m. p. 103°, was obtained from the 1 : 5-dichloronaphthalene-sulphonyl chloride, m. p. 141° (A. and W., Proc., 1890, 81), constituting the chief product (92·5%) * of the sulphonation of 1 : 5-dichloronaphthalene, and its identity with the product from Widman's 2 : 4-dichloronaphthalene-8-sulphonyl chloride, m. p. 148° (*Ber.*, 1882, 2160) established.

On sulphonation with chlorosulphonic acid (15 g.), the 1 : 3 : 5-trichloronaphthalene (28 g.) gave a product which solidified on completion of the interaction. From the aqueous solution unchanged trichloro-derivative (2·5 g.) was recovered, and non-volatile insoluble by-product (4·9 g.) collected, the latter proving to be mainly the *sulphone*, which crystallised from xylene in slender needles, m. p. above 305° (Found: Cl, 39·1. $C_{20}H_8O_2Cl_6S$ requires Cl, 40·5%). The *barium* salt crystallised in sparingly soluble, fern-like forms (Found: Ba, 17·7; H_2O, 5·8. $C_{20}H_8O_6Cl_6S_2Ba,2·5H_2O$ requires Ba, 17·1; H_2O, 5·6%); the *potassium* salt in clusters of hair-like, anhydrous needles (Found: K, 11·1. $C_{10}H_4O_3Cl_3SK$ requires K, 11·2%); and the *sulphonyl chloride* from benzene in highly soluble, elongated prisms, m. p. 152° (Found: Cl, 43·1. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%). Search for an isomeride proved fruitless. When heated with phosphorus pentachloride (40 g.) at 197—206° during 2·5 hours, the chloride (29 g.) was converted into a *tetrachloronaphthalene* (18·7 g.), which crystallised from alcohol in slender needles, m. p. 179° (Found: Cl, 53·5. $C_{10}H_4Cl_4$ requires Cl, 53·4%) and did not depress the m. p. of the tetrachloro-derivative, m. p. 179°, obtained from 1 : 3 : 7-trichloronaphthalene (p. 254), thus proving each to be the 1 : 3 : 5 : 7-compound.

VIII. 1 : 3 : 6 (2 : 5 : 7)-*Trichloronaphthalene.*

The 1 : 3 : 6-trichloronaphthalene, m. p. 80·5°, used was obtained from Alén's 1-nitronaphthalene-3 : 6-disulphonyl chloride, m. p. 138° (A. and W., Proc., 1895, 81). By interaction with chlorosulphonic acid (17 g.) this trichloronaphthalene (30 g.) furnished a solid product, from the aqueous solution of which unchanged trichloronaphthalene (4·1 g.) was recovered, and an insoluble, non-volatile material (0·6 g.) collected. The *barium* salt crystallised in anhydrous, sparingly soluble, irregular prisms (Found: Ba, 17·8. $C_{20}H_8O_6Cl_6S_2Ba$ requires Ba, 18·1%); the *potassium* salt in short needles (Found: K, 10·6; H_2O, 4·9. $C_{10}H_4O_3Cl_3SK,H_2O$ requires K, 10·6; H_2O, 4·9%); the *sodium* salt in moderately soluble, long, slender needles (Found: Na, 6·3; H_2O, 7·0. $C_{10}H_4O_3Cl_3SNa,1·5H_2O$ requires Na, 6·4; H_2O, 7·5%); and the *sulphonyl chloride* from benzene in easily soluble, long, four-sided prisms, m. p. 156° (Found: Cl, 43·1. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%). When heated with phosphorus pentachloride (28 g.) at 194—199° during 2·5 hours, the chloride (18·5 g.) gave a *tetrachloronaphthalene* (15·3 g.), which crystallised from alcohol in thin, flat needles, m. p. 119° (Found: Cl, 53·3. $C_{10}H_4Cl_4$ requires Cl, 53·4%). It distilled unusually rapidly with steam, 1 g. passing over in 6 hours with 3·2 l. of water, and did not depress the m. p. of the 1 : 3 : 6 : 7-tetrachloro-derivative, m. p. 120°, obtained from 2 : 3 : 6-trichloronaphthalene (p. 257).

IX. 1 : 3 : 7 (2 : 6 : 8)-*Trichloronaphthalene.*

The source of this trichloronaphthalene, m. p. 113°, was the 2-chloronaphthalenedisulphonyl chloride, m. p. 170°, obtained from 2-aminonaphthalene-6 : 8-disulphonic acid (amino-G-acid). It was sulphonated (30 g.) with chlorosulphonic acid (17 g.) and although the amount of unchanged substance was negligible, much non-volatile, insoluble "sulphone" (6 g.) emerged from each experiment made. The *barium* salt crystallised in sparingly soluble needles (Found: Ba, 17·0; H_2O, 7·8. $C_{20}H_8O_6Cl_6S_2Ba,3·5H_2O$ requires Ba, 16·7; H_2O, 7·7%); the *potassium* salt in sparingly soluble clusters of small needles (Found: K, 10·8; H_2O, 2·5. $C_{10}H_4O_3Cl_3SK,0·5H_2O$ requires K, 10·9; H_2O, 2·5%); the *sodium* salt in somewhat sparingly soluble scales (Found: Na, 6·1; H_2O, 11·0. $C_{10}H_4O_3Cl_3SNa,2·5H_2O$ requires Na, 6·1; H_2O, 11·9%); and the *sulphonyl chloride* from benzene in star-like clusters of prismatic needles, m. p. 138° (Found: Cl, 43·2. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%). When heated with phosphorus pentachloride (20 g.) at 188—195° during 1·5 hours, the chloride (27 g.) was converted into a *tetrachloronaphthalene* (14 g.),

* From the minor product of the sulphonation of 1 : 5-dichloronaphthalene hitherto not isolated (A. and W., *loc. cit.*), the isomeric *dichloronaphthalenesulphonyl chloride*, m. p. 125°, was obtained (Found: Cl, 35·8. $C_{10}H_5O_2Cl_3S$ requires Cl, 36·1%), which gave 1 : 2 : 5-trichloronaphthalene, m. p. 79° (p. 251) when heated with phosphorus pentachloride at 190—192°; *sodium* 1 : 5-*dichloronaphthalene*-2-*sulphonate* crystallising in long thin scales (Found: Na, 7·2; H_2O, 6·1. $C_{10}H_5O_5Cl_2SNa,H_2O$ requires Na, 7·3; H_2O, 5·7%); and 1 : 5-dichloronaphthalene on hydrolysis with superheated steam.

which crystallised from alcohol in sparingly soluble, long needles, m. p. 179° (Found: Cl, 53·3. $C_{10}H_4Cl_4$ requires Cl, 53·4%), and did not depress the m. p. of the 1 : 3 : 5 : 7-tetrachloro-derivative obtained from 1 : 3 : 5-trichloronaphthalene (p. 253).

X. 1 : 3 : 8-*Trichloronaphthalene.*

The trichloronaphthalene, m. p. 89·5 and 84°, was obtained from 1-chloronaphthalene-3 : 8-disulphonyl chloride, m. p. 110°, itself prepared from [ε-] acid (1-aminonaphthalene-3 : 8-disulphonic acid). For the sulphonation of this trichloronaphthalene (28 g.) chlorosulphonic acid (16 g.) was employed and from the aqueous solution of the solid product 0·6 g. of unchanged trichloro-derivative was recovered and 0·2 g. of insoluble, non-volatile material collected. The *barium* salt crystallised in sparingly soluble groups of very small needles (Found: Ba, 16·5; H_2O, 6·7. $C_{20}H_8O_6Cl_6S_2Ba,3H_2O$ requires Ba, 16·9; H_2O, 6·7%); the *potassium* salt in clusters of slender needles (Found: K, 10·2; H_2O, 7·2. $C_{10}H_4O_3Cl_3SK,1·5H_2O$ requires K, 10·4; H_2O, 7·2%); the *sodium* salt in long, slender, flat needles (Found: Na, 6·4; H_2O, 7·5. $C_{10}H_4O_3Cl_3SNa,1·5H_2O$ requires Na, 6·4; H_2O, 7·5%); and the *sulphonyl chloride* from benzene in easily soluble clusters of thin, four-sided plates, m. p. 127° (Found: Cl, 42·4. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%). When heated with phosphorus pentachloride (35 g.) at 172—185° during 2 hours, the chloride (30 g.) was converted into a *tetrachloronaphthalene* (18 g.) which crystallised from alcohol in slender needles, m. p. 131° (Found: Cl, 53·6. $C_{10}H_4Cl_4$ requires Cl, 53·4%), and did not depress the m. p. of the 1 : 3 : 5 : 8-tetrachloro-derivative obtained from 1 : 4-dichloronaphthalene tetrachloride, m. p. 172° (p. 246). Search for the presence of an isomeride proved fruitless. On hydrolysis, the potassium salt regenerated 1 : 3 : 8-trichloronaphthalene, which fused at 89·5° but in the translucent form at 85°.

XI. 1 : 4 : 7-*Trichloronaphthalene.*

This trichloronaphthalene, m. p. 68° in the ordinary opaque form but 58° when translucent—a condition seldom lasting more than 20 minutes—was obtained from 1 : 7-dichloronaphthalene-sulphonyl chloride, m. p. 119°, which, when crystallised from benzene, separated in long, transparent, prismatic needles, becoming opaque on exposure to the air owing to loss of "benzene of crystallisation" (Found: C_6H_6, by loss, 11·9. $C_{20}H_{10}O_4Cl_6S_2,C_6H_6$ contains C_6H_6, 11·6%).

Sulphonation with chlorosulphonic acid (12 g.) converted 1 : 4 : 7-trichloronaphthalene (21 g.) into a solid product, from which in aqueous solution 4 g. of unchanged trichloronaphthalene were recovered and 0·3 g. of insoluble, non-volatile residue was collected. The *barium* salt crystallised in sparingly soluble, anhydrous needles (Found: Ba, 17·7. $C_{20}H_8O_6Cl_6S_2Ba$ requires Ba, 18·1%); the *potassium* salt usually separated from water in a gelatinous form which, when redissolved, gave short, prismatic needles on the addition of an equal bulk of alcohol (Found: K, 10·7; H_2O, 5·1. $C_{10}H_4O_3Cl_3SK,H_2O$ requires K, 10·6; H_2O, 4·9%); the *sodium* salt likewise formed either a jelly or sparingly soluble lustrous scales (Found: Na, 6·5; H_2O, 5·2. $C_{10}H_4O_3Cl_3SNa,H_2O$ requires Na, 6·5; H_2O, 5·1%); and the *sulphonyl chloride* crystallised from benzene in easily soluble, small needles, m. p. 144° (Found: Cl, 42·7. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%). When heated with phosphorus pentachloride (27 g.) at 190—195° during 2 hours, the chloride (20 g.) was converted into 1 : 4 : 7 : (?)-*tetrachloronaphthalene*, which crystallised from alcohol in long, flat needles, m. p. 109° (Found: Cl, 53·3. $C_{10}H_4Cl_4$ requires Cl, 53·4%), and distilled rapidly with steam, 1 g. passing over in 6·6 hours.

XII. 1 : 4 : 8 (1 : 4 : 5)-*Trichloronaphthalene.*

The trichloronaphthalene, m. p. 131°, was obtained in good yield from 1-chloronaphthalene-4 : 8-disulphonyl chloride, m. p. 135° (A. and W., Proc., 1890, 127), by interaction with phosphorus pentachloride (3 mols.) at 195—215° during 2 hours, but when the proportion was reduced to 1 mol. and a temperature no higher than 160—170° maintained during 4—5 hours, intermediate derivatives were present in the product and much disulphonyl chloride remained unchanged. In three experiments, for example, in each of which the disulphonyl chloride (35 g.) was heated with phosphorus pentachloride (20 g.) under the latter conditions, the amounts of crude trichloronaphthalene isolated were 7, 5, and 5 g. (yielding a total weight of 11·9 g., m. p. 131°) and of potassium dichloronaphthalenesulphonate obtained were 7·3, 8·2, and 7·9 g. respectively. From the latter (23·4 g.), dissolved in 1·5 l. of boiling water, barium chloride in slight excess (8·5 g.) precipitated in the approximate ratio of 3 : 1 the less soluble *barium* salt as anhydrous needles (Found: Ba, 19·4. $C_{20}H_{10}O_6Cl_4S_2Ba$ requires Ba, 19·9%) from the more soluble *barium* salt, which crystallised from the hot filtrate, on cooling, in thin, small plates (Found:

Ba, 18·4; H_2O, 5·0. $C_{20}H_{10}O_6Cl_4S_2Ba,2H_2O$ requires Ba, 18·9; H_2O, 5·0%). Both potassium salts were anhydrous.

1 : 8-*Dichloronaphthalene*-4-*sulphonic Acid*.—The *sodium* salt, obtained from the less soluble barium salt, crystallised in somewhat sparingly soluble scales or short prismatic needles (Found : Na, 7·3; H_2O, 3·5. $C_{10}H_5O_3Cl_2SNa,0{\cdot}5H_2O$ requires Na, 7·5; H_2O, 2·9%), and the *sulphonyl chloride* from benzene, on addition of petrol, in small prisms, m. p. 117° (Found : Cl, 35·7. $C_{10}H_5O_2Cl_3S$ requires Cl, 36·1%), which did not depress the m. p. 116° of an authentic specimen prepared from 1 : 8-dichloronaphthalene (A. and W., Proc., 1890, 81) and when heated with phosphorus pentachloride furnished 1 : 4 : 8-trichloronaphthalene (m. p. 131°).

1 : 4-*Dichloronaphthalene*-8-*sulphonic Acid*.—The anhydrous *sodium* salt crystallised in easily soluble, thin, lustrous scales (Found : Na, 7·7. $C_{10}H_5O_3Cl_2SNa$ requires Na, 7·7%), and the *sulphonyl chloride* from benzene, on addition of petrol, in small prismatic needles often coated with minute, crystalline spherules, both of which had m. p. 96° (Found : Cl, 35·8. $C_{10}H_5O_2Cl_3S$ requires Cl, 36·1%). When heated with phosphorus pentachloride, the chloride was converted into 1 : 4 : 8-trichloronaphthalene (m. p. 131°) and therefore, by exclusion, the acid must have the constitution assigned.

When sulphonated with chlorosulphonic acid (12 g.), the 1 : 4 : 8-trichloronaphthalene (21 g.) gave a liquid product, from which unchanged material (3·3 g.) was recovered; a non-volatile, insoluble residue (2·2 g.) collected; and the sodium sulphonate obtained. After conversion of this salt into sulphonyl chloride two isomerides were identified by its fractional crystallisation, although their complete separation involved not only regeneration of sodium salt of each from these fractions, but its fractional precipitation by barium chloride, followed by reconversion into chloride. In a second preparation the order was reversed and the fractionation begun with the aid of barium chloride, but no advantage accrued.

Apart from various fractions (7·2 g.), m. p. 74—101°, from which a uniform constituent could not be isolated by these means, two chlorides were eventually separated, one of which fused at 118° (24·7 g.) and the other at 178° (4·3 g.).

The *sulphonyl chloride*, m. p. 118°, crystallised from benzene on addition of much petrol in small clusters of minute needles (Found : Cl, 42·7. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%), and the derived *sodium* salt in moderately soluble, long needles (Found : Na, 6·3; H_2O, 6·2. $C_{10}H_4O_3Cl_3SNa,1{\cdot}25H_2O$ requires Na, 6·5; H_2O, 6·3%). Heated with phosphorus pentachloride (20 g.) during 1·5 hours at 180—210°, the chloride (15 g.) gave a *tetrachloronaphthalene* (9·4 g.) which distilled only slowly with steam, 1 g. passing over in 12 hours with 5·9 l. of water. It crystallised from alcohol in long, slender needles, m. p. 131° (Found : Cl, 53·2. $C_{10}H_4Cl_4$ requires Cl, 53·4%), and did not depress the m. p. of the tetrachloronaphthalene, m. p. 131°, obtained from 1 : 3 : 8-trichloronaphthalenesulphonyl chloride, thus proving each to be the 1 : 3 : 5 : 8-derivative (p. 254).

The *sulphonyl chloride*, m. p. 178°, separated from light petroleum (b. p. 80—100°) in small crystalline aggregates (Found : Cl, 43·1. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%), and the derived *sodium* salt in masses of very slender needles from a slightly alkaline solution, but otherwise as a jelly (Found : Na, 6·5; H_2O, 7·3. $C_{10}H_4O_3Cl_3SNa,1{\cdot}5H_2O$ requires Na, 6·4; H_2O, 7·5%). The corresponding 1 : 4 : 8 : (?)-*tetrachloronaphthalene* crystallised from alcohol in long, slender, flexible needles, m. p. 144° (Found : Cl, 53·0. $C_{10}H_4Cl_4$ requires Cl, 53·4%), and was less volatile with steam than its isomeride, 1 g. passing over in 22·8 hours with 9·9 l. of water.

XIII. 2 : 3 : 5-*Trichloronaphthalene*.

The 2 : 3 : 5-trichloronaphthalene, m. p. 109°, was obtained from 2 : 3-dichloronaphthalene-5-sulphonyl chloride, m. p. 142° (A. and W., Proc., 1890, 83; 1895, 79), by interaction with phosphorus pentachloride.

On sulphonation with chlorosulphonic acid (6 g.), the trichloronaphthalene (12 g.) furnished a solid, from which only negligible amounts of the unchanged substance (0·2 g.) and an insoluble non-volatile by-product (0·6 g.) were collected. The *barium* salt crystallised in prismatic needles (Found : Ba, 16·4; H_2O, 7·1. $C_{20}H_8O_6Cl_6S_2Ba,3H_2O$ requires Ba, 16·9; H_2O, 6·7%); the *potassium* salt in flat needles arranged in leaf-like forms (Found : K, 10·6; H_2O, 4·7. $C_{10}H_4O_3Cl_3SK,H_2O$ requires K, 10·6; H_2O, 4·9%); and the *sulphonyl chloride* from benzene in clusters of needles which, after removal from the solvent, rapidly became opaque without appreciable loss of weight, but from light petroleum (b. p. 80—100°) in small prisms which remained transparent even after prolonged exposure, m. p. 164° (Found : Cl, 43·0. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%). No isomeride was found.

When heated with phosphorus pentachloride (13 g.) at 195—220° during 1·5 hours, the chloride (9·5 g.) was converted into *tetrachloronaphthalene* (7·3 g.), which distilled only slowly with steam, 1 g. passing over in 13 hours with 6·2 l. of water. It crystallised from alcohol in sparingly soluble, small prisms, mingled later with radiate groups of long needles, but from ligroin in prisms free from needles (Found: Cl, 52·4. $C_{10}H_4Cl_4$ requires Cl, 53·4%). Each form had at first the m. p. *ca.* 136° and solidified on cooling to a translucent mass which if heated immediately had m. p. 134°, but when kept for a short time became opaque and then fused at 139°. As a mixture of this tetrachloronaphthalene with that obtained from 1 : 4-dichloronaphthalene tetrachloride, m. p. 172°, by distillation (p. 246) behaved similarly under these conditions, it follows that each is the 2 : 3 : 5 : 8-derivative.

XIV. 2 : 3 : 6 (2 : 3 : 7)-*Trichloronaphthalene.*

The 2 : 3 : 6-trichloronaphthalene (m. p. 91°) first used was prepared from 2 : 7-dichloronaphthalene by sulphonation with chlorosulphonic acid. Two acids were obtained, the chief product furnishing by the usual method the 2 : 7-*dichloronaphthalene-3-sulphonyl chloride*, m. p. 166° (Found: Cl, 35·9. $C_{10}H_5O_2Cl_3S$ requires Cl, 36·1%), and its isomeride—mentioned but not described by Armstrong and Wynne (Proc., 1890, 84)—the 2 : 7-*dichloronaphthalene-4-sulphonyl chloride*, m. p. 152° (Found: Cl, 35·9. $C_{10}H_5O_2Cl_3S$ requires Cl, 36·1%), constituting about 10% of the product and convertible into 1 : 3 : 6 (2 : 4 : 7)-*trichloronaphthalene*, m. p. 81° (Found: Cl, 46·4. $C_{10}H_5Cl_3$ requires Cl, 46·0%).

Subsequently, 2-aminonaphthalene-3 : 6-disulphonic acid (amino-R-acid)—for a supply of which we were indebted to Imperial Chemical Industries (Dyestuffs), Ltd., Blackley, Manchester—became the source. From the derived 2-chloronaphthalene-3 : 6-disulphonyl chloride, m. p. 166° (50 g.), by interaction with phosphorus pentachloride (58 g.) at 195—207° during 2 hours there was obtained in addition to 2 : 3 : 6-trichloronaphthalene (17·7 g.) and unchanged sodium 2-chloro-3 : 6-disulphonate (14·4 g.) a small yield of *sodium* 2 : 6-*dichloronaphthalene-3-sulphonate* (4·3 g.), crystallising in nacreous scales (Found: Na, 5·7; H_2O, 22·9. $C_{10}H_5O_3Cl_2SNa,5H_2O$ requires Na, 5·9; H_2O, 23·1%), which on hydrolysis with hydrochloric acid at 260° gave 2 : 6-dichloronaphthalene (m. p. 136°). The *sulphonyl chloride* separated from benzene, after addition of petrol, in flat needles, m. p. 131° (Found: Cl, 35·9. $C_{10}H_5O_2Cl_3S$ requires Cl, 36·1%), and when heated with phosphorus pentachloride was converted into 2 : 3 : 6-trichloronaphthalene. No trace of the isomeric 2 : 3-dichlorosulphonate was found.

On sulphonation with chlorosulphonic acid (12·5 g.) the 2 : 3 : 6-trichloronaphthalene (23 g.) gave a solid product, from which unchanged trichloro-derivative (2·6 g.) was recovered and insoluble substance (0·3 g.) collected. From the barium salt two sodium salts were obtained, one crystallising in sparingly soluble, long, slender, glistening needles (12·9 g.) and the other in easily soluble, short needles (14·1 g.). Both proved to be mixtures on conversion into sulphonyl chloride, the former giving mainly small rhombs (8·4 g.), m. p. *ca.* 114°, mixed with needles, m. p. 109—113°; the latter, needles in tufts, m. p. 111—112°, later raised by purification to 118° (10·9 g.), mixed in the final separations with minute rhombs (1·5 g.) removable by sieving. But whereas the chloride, m. p. 118°, when heated with phosphorus pentachloride gave a uniform tetrachloronaphthalene, m. p. 120°, that in rhombs, m. p. 114°, characterised by setting to a glass on cooling, gave two tetrachloro-derivatives, of which one had m. p. 112° (later by purification raised to 120°) and the other m. p. 218°—these respectively in the proportion of *ca.* 3 : 1. On this evidence, the rhombic form, although well defined, was a mixture of the chloride, m. p. 118°, with the constituent yielding the tetrachloronaphthalene, m. p. 218°, but only after several failures did it prove possible to achieve a separation by fractionation of the regenerated sodium salt, followed by reconversion of each fraction into chloride—14·9 g. of the rhombs giving the chloride, m. p. 118° (4·3 g.); rhombs, m. p. 114° (1·8 g.); intermediate fractions, m. p. 100—109° (1·1 g.); and from the least soluble salt the elusive isomeride, m. p. 94° (3·4 g.). The rhombic form, m. p. 114° (0·136 g.), was the only substance to crystallise from a solution of equal weights (0·075 g.) of the isomeric chlorides in benzene–petrol.

The *sulphonyl chloride*, m. p. 94°, crystallised from benzene, on addition of petrol, in tufts of long slender needles (Found: Cl, 42·8. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%); the *barium* salt in very sparingly soluble, minute prisms (Found: Ba, 16·6; H_2O, 6·4. $C_{20}H_8O_6Cl_6S_2Ba,3H_2O$ requires Ba, 16·9; H_2O, 6·7%); and the *sodium* salt in sparingly soluble bundles of very slender needles (Found: Na, 6·4; H_2O, 5·3. $C_{10}H_4O_3Cl_2SNa,H_2O$ requires Na, 6·5; H_2O, 5·1%). The chloride (1·6 g.), when heated with phosphorus pentachloride (2·2 g.) at 180—

190° during an hour, gave a 2 : 3 : 6 : (?)-*tetrachloronaphthalene* (1·1 g.), which crystallised from alcohol in sparingly soluble, long, slender needles, m. p. 218° (Found : Cl, 53·3. $C_{10}H_4Cl_4$ requires Cl, 53·4%). On distillation with steam, 1·0 g. passed over with 18·6 l. of water in 28 hours.

The *sulphonyl chloride*, m. p. 118°, crystallised from benzene on the addition of petrol in aggregates of small flat prisms (Found : Cl, 43·1. $C_{10}H_4O_2Cl_4S$ requires Cl, 43·0%); the *barium* salt in very sparingly soluble minute rods (Found : Ba, 16·5; H_2O, 7·6. $C_{20}H_8O_6Cl_6S_2Ba,3·5H_2O$ requires Ba, 16·7; H_2O, 7·7%); the *sodium* salt in moderately soluble, thin, nacreous scales (Found : Na, 6·1; H_2O, 7·9. $C_{10}H_4O_3Cl_3SNa,1·5H_2O$ requires Na, 6·4; H_2O, 7·5%). The chloride (5·7 g.), heated with phosphorus pentachloride (8 g.) at 190—210° during 1·5 hours, gave a *tetrachloronaphthalene* (3·1 g.) readily soluble in alcohol, which crystallised in short, slender needles, m. p. 120° (Found : Cl, 53·5. $C_{10}H_4Cl_4$ requires Cl, 53·4%), and did not depress the m. p. of the tetrachloronaphthalene, m. p. 119°, obtained from 1 : 3 : 6-trichloronaphthalene (p. 254), whence the orientation 1 : 3 : 6 : 7 was assigned to both. On distillation with steam, 1 g. was collected together with 3·4 l. of water in 6·7 hours. Its *nitro*-derivative separated from alcohol in easily soluble, short needles, m. p. 145° (Found : N, 4·4; Cl, 45·5. $C_{10}H_3O_2NCl_4$ requires N, 4·5; Cl, 45·7%).

Cordial acknowledgment is made by one of us to the Management Committee of the University Chemical Laboratory, Cambridge, for the facilities which have made the completion of this investigation possible.

THE UNIVERSITY, SHEFFIELD.
UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, February 13th*, 1941.]

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44. *The Salts of Diphenic Acid with Optically Active Bases.*

By MARY S. LESSLIE, E. E. TURNER, and E. R. WINTON.

The specific rotation of quinine diphenate in alcohol–chloroform has an unusually high temperature coefficient. This was responsible for certain apparent mutarotations described previously. At −30°, diphenic acid undergoes rapid optical activation in chloroform or acetone–chloroform in presence of nor-*d*-ψ-ephedrine.

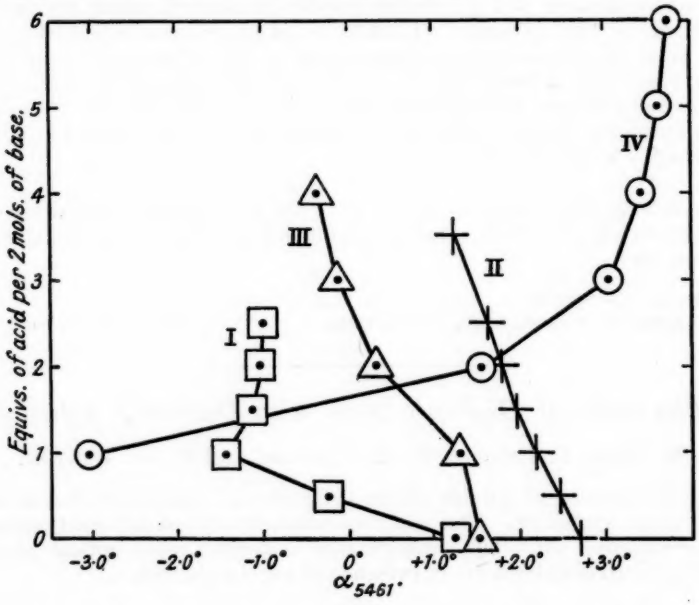
IN a previous communication (Lesslie and Turner, J., 1934, 347) certain alkaloidal salts of diphenic acid were described as exhibiting slight mutarotation in alcoholic or alcohol–chloroform solution, and it was inferred that asymmetric induction was responsible for the effects observed, and was made possible by the low optical stability of diphenic acid. Further examination of the problem has now shown that the specific rotation of quinine diphenate has an unusually high temperature coefficient, and that the " mutarotation " described in 1934 was due to this. The following figures were obtained for a solution of quinine diphenate alcoholate in a mixture of ethyl alcohol (2 vols.) and chloroform (1 vol.) ($l = 4$; $c = 4·472$) :

Temp.	0·8°	20·1°	24·8°	29·5°	35·4°	39·5°	43·1°	45·5°
α_{5791}	+ 9·14°	+ 8·36°	+ 7·99°	+ 7·48°	+ 6·93°	+ 6·19°	+ 5·62°	+ 5·23°
α_{5461}	+10·54°	+ 9·75°	+ 9·31°	+ 8·70°	+ 8·03°	+ 7·18°	+ 6·55°	+ 6·07°

Corresponding figures were obtained several times, and on no occasion was mutarotation observed at any temperature within the above limits. Again, solutions of mixtures of equivalent proportions of quinine and diphenic acid also exhibited no motarotation when rigid temperature control was exercised. Our new results thus agree with those of Kharasch, Senior, Stanger, and Chenicek (*J. Amer. Chem. Soc.*, 1934, **56**, 1646). We are permitted to say that Dr. Breckenridge, in a private communication to Professor McKenzie (Jan. 16th, 1940), has stated that the mutarotation observed by Breckenridge and Smith (J., 1939, 1536) with alkaloidal salts of 2-phenylpyridine-2' : 3-dicarboxylic acid is also due solely to a temperature effect, no mutarotation in the real sense of the word being involved (compare McKenzie and Wood, J., 1939, 1536).

Since the appearance of our 1934 paper, a method (Jamison and Turner, J., 1938,

1646; 1940, 264) has become available for the detection of the optical activity of optically unstable acids, and we have therefore applied it to the examination of diphenic acid. By adding diphenic acid in continually increasing quantities to a chloroform solution of nor-*d*-ψ-ephedrine, addition curve (I) was obtained, and for acetone and mixtures of acetone (1 vol.) and chloroform (4 vols.) addition curves (II) and (III), respectively, were constructed. From curve (I) it may be inferred that when diphenic acid is present in excess over the base, optical activation occurs, and results in the formation of a preponderance of the *d*-base *d*-acid salt. In acetone (curve II) and in acetone–chloroform (curve III), the *d*-base *l*-acid salt would appear to be formed in excess.



We then applied the test of rapidly mixing solutions of acid and base (*a*) in chloroform and (*b*) in acetone–chloroform at − 30° in the apparatus used previously (Jamison and Turner, *loc. cit.*). In a 2-dcm. tube, the following observations were made:

(*a*) Chloroform solution. 0·2 G. of nor-*d*-ψ-ephedrine in 5 c.c. of chloroform mixed with 0·5 g. of diphenic acid in 30 c.c. of chloroform:

Time after mixing (mins.)	0·17	0·45	0·75	1·25	1·55	4·5
Observed angle (λ 5461)	+0·15°	+0·30°	+0·35°	+0·40°	+0·42°	+0·42°

(*b*) Chloroform (4 vols.)–acetone (1 vol.) solution. 0·15 G. of nor-*d*-ψ-ephedrine in 3 c.c. of chloroform, mixed with 0·3 g. of diphenic acid in 20 c.c. of chloroform + 5 c.c. of acetone:

Time after mixing (mins.)	0·15	0·60	1·20	2·95	6·15
Observed angle (λ 5461)	−0·76°	−0·94°	−1·02°	−1·10°	−1·10°

In the apparatus used, it is quite impossible to make a polarimetric reading unless thermal homogeneity is complete, and the observed mutarotations are therefore unequivocal evidence of rapid optical activation. This observation must be taken as indicating that, at − 30°, diphenic acid, or at any rate the diphenate ion in electrostatic combination with the nor-*d*-ψ-ephedrinium ion, has a perceptible optical stability. From the extremely low optical stability of the nor-*d*-ψ-ephedrine salts of diphenic acid at − 30°, it must, however, be inferred that, although at room temperature optical activation of diphenic acid in presence of optically active bases might be detectable by the addition curve technique, yet it is equally clear that no mutarotation could be expected whatever the nature of the base used.

The addition curve (IV) for cinchonine and diphenic acid indicates that base *d*-acid is considerably more stable than base *l*-acid in acetone solution. Owing to the sparing solubility of cinchonine in this solvent, its rotation does not appear on the curve, and for a similar reason it was impracticable to carry out experiments at low temperatures.

When nor-*d*-ψ-ephedrine is dissolved in acetone, mutarotation occurs. Thus, in obtaining the data for curve (II), α_{5461} changed during an hour at room temperature from + 2·13° to + 2·69°, whilst in the case of curve (III) it changed from + 1·20° to + 1·55°. The final values are given on the curves. These mutarotations do not invalidate the above conclusions drawn from the addition curves, since the salt, nor-*d*-ψ-ephedrine diphenate, does not give rise, at the ordinary temperature, to mutarotation in either of the solvents concerned.

One of us (E. R. W.) thanks the Carnegie Trust for the Universities of Scotland for the award of a scholarship.

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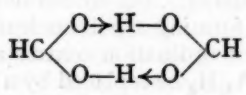
45. *Molecular Compounds of Phenylacetic Acid and its Salts. Part I. A Covalent Compound of Sodium.*

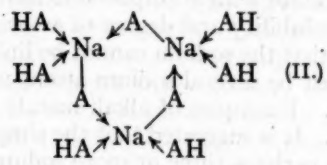
By MALCOLM CRAWFORD.

An acid " salt " of the composition NaA,2HA (A = $CH_2Ph{\cdot}CO{\cdot}O{\cdot}$) has been prepared. Although it contains sodium, it is readily soluble in benzene and other organic solvents. The binary system NaA–HA has been studied, and molecular-weight determinations of the compounds have been made in various solvents. Acid sodium salts of benzoic and cinnamic acids, which, however, are not soluble in organic solvents, as well as other molecular compounds of sodium phenylacetate, have also been isolated.

IT has long been known that many monobasic carboxylic acids form acid salts (for summary, see Ross and Morrison, J., 1933, 1016). Many of the acids themselves, such as benzoic, cinnamic, and phenylacetic, have been shown to exist as double molecules in solution (Pound and Pound, *J. Physical Chem.*, 1933, **37**, 971) and in the gaseous state. Pauling and Brockway (*Proc. Nat. Acad. Sci.*, 1924, **20**, 336) ascribe the structure (I) to formic acid vapour, but in order to account for the solubility in organic solvents it is assumed that the acid " salt " in question has a structure different from those of associated acids, in that it may not be held together by the hydrogen bond, but by co-ordination to a central metal atom, or, as is more likely from the molecular-weight determinations, to several metal atoms forming a polynuclear complex.

The majority of acid salts described in the literature are potassium salts, those of sodium being rarer. This is apparently only due to preparative difficulties, the sodium salts being generally more soluble and difficult to crystallise. Acid sodium *salts* have now been prepared from phenylacetic, benzoic, and cinnamic acids; the molar ratios of salt to acid for the first two acids respectively are 1 : 2 and 1 : 3, whereas the last acid forms derivatives of both types (phenylacetic acid may also form a 2 : 1 compound). Landrieu (*Compt. rend.*, 1920, **170**, 1452) has described an acid benzoate of the 1 : 2 composition, but this could not be confirmed. Both the cinnamates seemed to have a lower order of stability

(I.) 



(II.)

and their compositions altered on recrystallisation; this did not apply to the benzoate or phenylacetate. Both cinnamates and the benzoate are insoluble in most organic

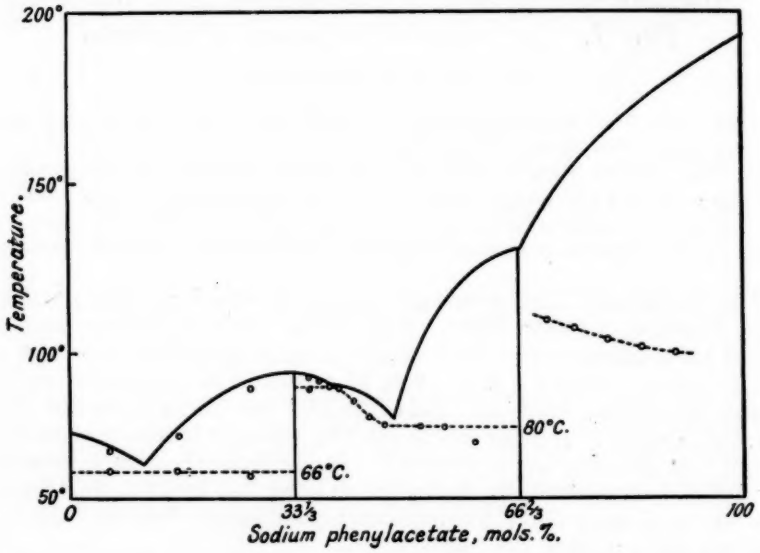
solvents but soluble in aqueous and hydroxylic solvents such as hot water, acetic acid, glycerol, and phenol. When the hot aqueous solution is cooled, the acid separates. The phenylacetate, however, is a substance of entirely different character. It consists of fine hair-like threads, m. p. 94·4°. It is not salt-like and is readily soluble in benzene, ether, and chloroform; it is also water-soluble.

The solubility of this compound in organic solvents renders possible the determination of its molecular weight cryoscopically. Table I gives the results obtained with various solvents, M being the apparent molecular weight (calc., 430·2), and α the degree of association. There is a wide variation from solvent to solvent. In hydrocarbon solution α

TABLE I.

Solvent.	Approx. f. p. of solvent.	M.	α.	Solvent.	Approx. f.p. of solvent.	M.	α.
Benzene	5°	1390	3·2	Benzophenone ...	49°	458	1·1
Diphenylmethane	26	807	1·9	Camphor	176	300	0·7
Naphthalene	81	658	1·5	Phenol	42	171	0·4

decreases with increasing temperature, which is to be expected from the flatness of the relevant portion of the curve representing the system acid–salt given in the figure. The



compound is obviously considerably dissociated at its m. p. In the hydroxylic solvent dissociation into acid and salt is complete at ordinary temperatures, probably owing to combination of phenol with the salt, for an equimolar *compound* has been isolated and analysed. (Sodium phenylacetate forms a dihydrate but not an alcoholate, as far as can be ascertained.) In ketones there is no association of NaA,2HA as in hydrocarbons, which probably means that some sort of combination is taking place with the ketone. No compound with benzophenone could be isolated, but a probable *compound* of sodium phenylacetate with acetophenone has been obtained, although it is unstable.

The solubility and degree of association of sodium acid phenylacetate in hydrocarbons indicate that the sodium cannot be linked by electrovalencies, but by covalencies, and that there must be several sodium atoms in the molecule, forming a polynuclear co-ordination complex. Examples of alkali metals functioning as co-ordination centres are known but are rare. It is suggested that the simple formula $[NaA_3]H_2$ be replaced by a more complex one with perhaps three or more sodium atoms, such as (II), in which each sodium atom is assumed to be 4-covalent.

Ross and Morrison (*loc. cit.*) investigated the acid salts of mandelic acid, but were

unable to study the binary systems acid–salt because of the instability of mandelic acid at and above its m. p.; they had to study the less satisfactory ternary systems acid–salt–water. These difficulties do not exist in the case of phenylacetic acid, and since sodium phenylacetate melts as low as 195° without decomposition except over long periods, the binary system has been examined by the determination of the m. p.'s of mixtures of the acid and salt. The results are given in Tables II and III and in the form of a diagram.

TABLE II.

Melting points of mixtures of acid and salt.

Salt, %.	M. p.	Salt, %.	M. p.	Salt, %.	M. p.	Salt, %.	M. p.	Salt, %.	M. p.	Salt, %.	M. p.
0·0	77·1°	27·0	92·3°	48·2	81·4°	64·6	128·9°	74·9	155·0°	89·0	180·1°
3·8	74·4	27·4	92·5	48·5	82·9	65·4	129·7	75·5	156·6	89·5	180·7
6·5	72·2	28·5	93·3	49·0	88·6	65·6	129·9	76·5	159·2	90·5	182·2
9·0	69·9	30·0	93·9	49·5	92·9	66·4	131·1	77·5	161·4	91·5	184·5
10·5	68·1	31·5	94·4	50·4	95·9	66·6	131·1	78·2	163·8	92·2	183·8
11·0	67·9	33·4	94·4	51·6	102·7	67·0	131·2	78·6	163·0	92·7	186·0
11·5	68·5	35·9	93·9	53·0	108·3	67·5	134·5	79·0	165·1	93·6	187·2
11·6	66·9	37·4	92·9	54·2	112·2	68·0	135·2	79·3	166·0	94·0	184·9
12·6	71·1	38·2	91·5	55·0	114·2	68·4	137·3	79·7	166·5	94·1	187·5
13·6	73·4	39·5	91·4	55·5	115·4	69·0	139·0	80·1	166·4	94·6	186·3
14·9	76·3	40·9	90·3	56·1	117·0	69·6	140·5	80·7	168·0	94·8	188·1
16·4	79·2	41·6	90·0	56·5	117·4	70·1	142·2	81·5	169·5	95·2	187·8
17·6	81·4	42·3	89·4	57·3	119·3	70·5	143·5	82·1	169·6	96·1	189·6
18·3	82·6	44·0	88·1	58·0	120·5	71·0	147·7	83·0	170·8	96·6	191·1
18·9	83·7	45·2	86·6	59·0	122·5	71·3	144·2	83·6	172·0	97·0	191·6
20·1	85·0	45·8	85·8	59·9	124·2	71·3	146·2	84·6	174·4	98·1	192·9
20·9	86·5	46·5	84·7	61·0	125·6	71·7	147·1	85·4	174·7	100·0	195·2
21·9	87·5	47·2	83·0	62·2	126·6	72·8	150·7	86·1	175·4		
24·0	90·0	47·4	81·6	62·9	127·4	73·9	153·3	86·9	177·6		
26·1	91·6	47·9	81·0	63·9	138·5	74·6	154·4	88·0	179·4		

Bakunin and Vitale (*Gazzetta*, 1935, **65**, 593) have already examined this system, but the results now obtained differ considerably from theirs; *e.g.*, they reported a third eutectic point between a compound of the composition HA,2NaA and NaA, whereas no eutectic depression is seen in the figure, and it is doubtful even whether this compound has a congruent m. p. Moreover, no compound of that composition could be isolated.

TABLE III.

Points of arrest in the cooling curves of mixtures of acid and salt.

Salt, %.	Liquidus arrest.	Solidus arrest.	Salt, %.	Liquidus arrest.	Solidus arrest.	Salt, %.	Liquidus arrest.	Solidus arrest.
5·9	72°	66°	41·9	—*	87°	64·8	—†	—
16·2	76	66	44·5	—*	82	71·0	—†	111°
26·9	90	65	46·5	—*	80	75·0	—†	108
35·5	93	90	48·0	—†	80	79·8	—†	105
37·0	—*	93	55·0	—†	79	85·0	—†	103
38·5	—*	91	59·9	—†	75	90·0	—†	102
40·0	—*	90						

* Only one arrest observed. † Liquidus arrest not determined.

The curve shows clearly the existence of the *compound* NaA,2HA and also two distinct eutectic points (67·5° at 11·1% of salt and 80·5° at 47·7% of salt).

The solidus portion of the diagram was determined by the cooling-curve method; hence with many mixtures the consequent supercooling and slow rate of crystallisation have caused many low results. In spite of this, the existence of the compounds NaA,2HA and HA,2NaA is substantiated. There is also strong evidence for the existence of a compound containing from 35 to 40% of salt. The liquidus line also shows some irregularity in this region. No such compound has been isolated, mixtures of this composition on recrystallisation invariably yielding NaA,2HA.

Mixtures of the composition HA,2NaA are not soluble in benzene or in other organic solvents, and recrystallisation from aqueous acetone or aqueous alcohol alters the com-

position. For this reason attempts to prepare a definite specimen of this compound failed.

Experimental.

The m. p.'s were determined upon about 0·5 g. of each mixture in an air-jacketed glass tube 3″ × 3/8″ in which a thermometer graduated in 0·5° was suspended, the whole being in a glycerol-bath of which the temperature could be raised or lowered extremely slowly. The cooling-curve method was not used owing to supercooling difficulties, it being possible to cool many of the mixtures to room temperature without crystallisation taking place. Instead, the m. p. was taken as the point at which, if a minute amount of the solid fused mixture were introduced on the tip of a glass needle with shaking, growth and not solution took place. In practice the needle was dipped into the fused liquid just above its m. p., withdrawn slightly above the liquid, allowed to cool sufficiently so that the drop of liquid solidified, and then reintroduced into the liquid. The growth or solution was observed through a lens. The m. p. so obtained proved to be identical within 0·1° with the point at which complete disappearance of crystals took place when the mixture, after fusion and solidification, was heated very slowly with agitation, a process requiring much more time. This simple method in which very small quantities were used gave remarkably consistent results, generally within 0·1°, except with certain mixtures, especially those in the vicinity of eutectic points, where increased viscosity reduced the rate of crystallisation.

Sodium Phenylacetate.—Concentrated aqueous sodium hydroxide was treated with a slight excess of alcoholic phenylacetic acid, and the mixture diluted with 10 vols. of alcohol, evaporated to small bulk, and diluted to the same volume with benzene. On concentrating, crystals separated which were recrystallised from slightly moist acetone. The resulting colourless needles of the dihydrate lose some water on standing in the air, and all of it quickly at 110°. The product is readily soluble in water or phenol, but only in alcohol and acetone after the addition of a trace of water [Found: *M* (cryoscopic in phenol), 144; (Rast method), 3300. Calc.: *M*, 158].

The Compound of Sodium Phenylacetate with Phenol.—Sodium carbonate (½ mol.) was added to a solution of phenylacetic acid (1 mol.) in phenol (2 mols.). The mixture was heated gently till all carbon dioxide had been evolved and was then allowed to cool. The solid mass was dissolved in carbon tetrachloride, and addition of light petroleum precipitated very hygroscopic needles, m. p. (in sealed tube) 105—125° (Found: PhOH, 36·8; $CH_2Ph{\cdot}CO_2H$, 53·8. $C_6H_5{\cdot}OH,C_6H_5{\cdot}CH_2{\cdot}CO_2Na$ requires PhOH, 37·3; $CH_2Ph{\cdot}CO_2H$, 54·0%).

The Compound of Sodium Phenylacetate with Acetophenone.—On cooling a hot solution of NaA in acetophenone, needles separated which were filtered off and dried on porous tile. The *substance* was decomposed into its constituents on treatment with water (Found: $CH_2Ph{\cdot}CO_2H$, 53·1; $CH_2Ph{\cdot}CO_2Na,C_6H_5{\cdot}CO{\cdot}CH_3$ requires $CH_2Ph{\cdot}CO_2H$, 48·9%). On recrystallisation from acetone, the substance lost acetophenone (Found: $CH_2Ph{\cdot}CO_2H$, 64·9%).

Sodium Acid Phenylacetate.—Sodium carbonate (½ mol.) was dissolved in a boiling benzene solution of phenylacetic acid (3 mols.). On concentration to small bulk and addition of excess of light petroleum, silky hair-like needles separated, which were recrystallised from benzene and light petroleum or from *cyclo*hexane, m. p. 94·4°, readily soluble in most organic solvents and in hot water (Found: $CH_2Ph{\cdot}CO_2H$, 63·1. $2C_8H_8O_2,C_9H_7O_2Na$ requires $C_8H_8O_2$, 63·2%). The values for the molecular weight of this *substance* given in Table I were determined by the Beckmann method, specially purified solvents being used.

Disodium Acid Phenylacetate.—NaA (2 mols.) and HA (1 mol.) were melted together and cooled, giving a crystalline mass. Powdered samples of this were insoluble in organic solvents, but soluble in moist acetone and in moist alcohol. The composition altered on recrystallisation from either of these, owing to loss of HA, becoming richer in NaA after each recrystallisation.

Possible Compound with 35—40% of Sodium Phenylacetate.—A mixture containing 40% of salt and 60% of acid was dissolved in benzene, and light petroleum added. The feathery crystals which separated after some time were found by titration to be pure NaA,2HA.

Sodium Acid Benzoate.—Sodium benzoate (1 mol.) was dissolved in the minimum amount of hot water, and benzoic acid (3 mols.) added together with sufficient acetone to dissolve it in hot solution. On cooling, needles separated which were recrystallised from acetone–water (5 : 1). The crystals melt at 227° in a sealed tube, and are insoluble in benzene, chloroform, or cold water. The solution in hot water deposits benzoic acid on cooling (Found: $C_6H_5{\cdot}CO_2H$, by titration, 70·4; Na, 4·5. $C_7H_5O_2Na,3C_7H_6O_2$ requires $C_6H_5{\cdot}CO_2H$, 71·7; Na, 4·5%).

Sodium Acid Cinnamates.—The two *compounds* were prepared by mixing solutions of cin-

namic acid (2 and 3 mols. severally) in hot acetone with sodium carbonate (½ mol.) in hot water. More acetone was added when necessary till solution was complete. After some concentration, large needles separated on cooling (Found: $C_9H_8O_2$, by titration, 62·9, 72·8, respectively. $C_9H_7O_2Na,2C_9H_8O_2$ requires $C_9H_8O_2$, 63·5%. $C_9H_7O_2Na,3C_9H_8O_2$ requires $C_9H_8O_2$, 72·3%). When heated in a sealed capillary tube, the substances did not melt below 300°, but crystals, probably of cinnamic acid, sublimed. In both cases water dissolved out sodium cinnamate, leaving pure cinnamic acid.

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46. *Retention of Asymmetry during the Curtius and the Beckmann Change.*

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(+)Hydratropic azide is converted by the Curtius rearrangement into (−)α-phenylethylamine with 99·3% retention of optical purity. The previously observed loss of 4·2% in optical purity during the analogous Hofmann rearrangement may be connected with the known racemisation of *iso*cyanates by alkalis. The oxime of (−)*methyl γ-heptyl ketone* undergoes the Beckmann transformation into (+)*aceto-γ-heptylamide*, apparently in an optically pure condition. Evidence is therefore presented that the Curtius and the Beckmann reaction also are true intramolecular rearrangements.

It is now possible to show that in the Hofmann, Curtius, Lossen, Beckmann, sulphinate, and (probably) alkylphenol rearrangements, the migrating group ·Cabc retains its relative configuration during transfer.

(I) A RECENT investigation (Arcus and Kenyon, J., 1939, 916) has shown that optically active hydratropamide, $CHMePh{\cdot}CO{\cdot}NH_2$, is converted by the Hofmann rearrangement into α-phenylethylamine with an average retention of 95·8% of optical activity. We now find that from the analogous Curtius rearrangement of the azide of (+)hydratropic acid is obtained (−)α-phenylethylamine of no less than 99·3% optical purity. In both these reactions the sign of rotation of the amine is the opposite of that of the original hydratropic acid.

The present result renders it probable that in the Curtius reaction no racemisation at all takes place during the migration of the optically active –CHMePh group, the observed loss of 0·7% probably being covered by experimental errors occasioned by the high temperature coefficients of the rotatory powers of the compounds concerned. A difference is therefore to be noted between the two rearrangements, as the 4·2% loss in optical purity observed by Arcus and Kenyon is real and outside the experimental error. In view of the close similarity between the Hofmann and the Curtius reaction, it seems unlikely that, in the former, migration is accompanied by the dissociation of a proportion of free –CHMePh radicals to bring about the observed racemisation. Some light is, however, cast on this phenomenon by Wallis and Dripps' observation (*J. Amer. Chem. Soc.*, 1933, **55**, 1701) that (+)α-benzylethyl *iso*cyanate was hydrolysed in acid solution to (+)α-benzylethylamine hydrochloride with no apparent racemisation, but that on alkaline hydrolysis it gave *dl-NN'*-bis-α-benzylethylurea. This suggests that, like optically active disubstituted acetic esters, *iso*cyanates of the type $CHRR'{\cdot}N{:}C{:}O$, which are intermediates in both the reactions under discussion, suffer racemisation in presence of an alkaline reagent such as is used to bring about the Hofmann reaction. In the Curtius reaction, on the other hand, the free *iso*cyanate is obtained directly without the action of a reagent and in the present instance was hydrolysed to the amine by means of hydrochloric acid.

The observed racemisation of *iso*cyanates by alkalis further strongly suggests that, as in the case of carboxylic esters (cf. Kenyon and Young, J., 1939, 216), these compounds under the influence of bases lose a proton from the α-carbon atom.

From these considerations it appears that during both the Hofmann and the Curtius

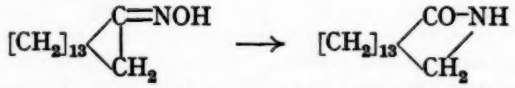
rearrangement, asymmetry of the migrating group –CHMePh is maintained quantitatively, thereby providing strong evidence that these reactions are truly intramolecular, and, in fact, that electron-sharing between the migrating group and the rest of the molecule is continuous throughout.

(II) We have also examined the stereochemical course of the Beckmann transformation of an optically active ketoxime CHRR'·CMe:NOH into the substituted acetamide CHRR'·NH·COMe.

The Beckmann change is a spontaneous rearrangement of oxime esters (of strong acids) or salts of oximes or their esters; the rearrangement of the oximes themselves by means of various reagents probably takes place through the medium of one of these compounds (Blatt, *Chem. Rev.*, 1933, **12**, 215; Watson, "Modern Theories of Organic Chemistry," 1937, p. 139):

$$R\cdot\underset{\underset{NOH}{|}}{C}\cdot R' \longrightarrow R\cdot\underset{\underset{NOX}{|}}{C}\cdot R' \xrightarrow{\text{direct}} XO\cdot\underset{\underset{NR}{|}}{C}\cdot R' \xrightarrow{H_2O} O{=}\underset{\underset{NHR}{|}}{C}\cdot R'$$

Entry of the migrating group into a foreign molecule has never been observed, but at present the only direct piece of evidence that the migrating group is never kinetically free is provided by an interesting ring enlargement carried out by Ruzicka and his co-workers (*Helv. Chim. Acta*, 1933, **16**, 1323):



If the ring were opened during the transformation, it would only close again to an extremely limited extent.

For the purpose of this investigation an optically active ketone of the type CHRR'·COMe was required. An attempt to resolve methyl β-butyl ketone directly by means of an alkaloidal salt of its o-*carboxyphenylhydrazone* was unsuccessful, and recourse was made to synthesis from the corresponding optically active acid CHRR'·CO_2H. Accordingly, the bromide of (—)ethyl-*n*-butylacetic acid was treated with dimethylcadmium in ethereal solution (Gilman and Nelson, *Rec. Trav. chim.*, 1936, **55**, 518), affording (—)*methyl γ-heptyl ketone*, which was converted into its dextrorotatory oxime. On treatment with phosphorus pentachloride the oxime underwent rearrangement to dextrorotatory *aceto-γ-heptylamide*, $[\alpha]^{21°}_{5461}$ + 1·4°, $[\alpha]^{21°}_{4358}$ + 5·3° (in alcohol). The constitution of the last compound was confirmed by synthesis of the corresponding dl-*amide*, by acetylating dl-*γ-heptylamine* obtained from *dl*-ethyl-*n*-butylacetamide by the Hofmann reaction; the product was identical with that from the dl-*oxime*, which therefore has the *anti*-heptyl structure. This observation is in harmony with the results of Bachmann and Barton (*J. Org. Chem.*, 1938, **3**, 300), who found that stable ketoximes were generally *anti*- with respect to the heavier group.

By using a partly resolved (+)ethylbutylacetic acid, a (—)aceto-γ-heptylamide was obtained similarly, having $[\alpha]^{21°}_{5461}$ — 0·7°, $[\alpha]^{21°}_{4358}$ — 1·2°. Starting from the same acid, the last compound was also obtained *via* γ-heptylamine as above, and this had $[\alpha]^{21°}_{5461}$ — 0·6°, $[\alpha]^{21°}_{4358}$ — 2·0°. Too much quantitative significance should not be given to these low rotations, but they are sufficient to determine the configurational relationships involved. Some evidence was obtained, however, that the *l*(+)aceto-γ-heptylamide must have been nearly optically pure, as it melted fairly sharply at 43—44·5°, whereas the partly active (—)amide melted lower and more indefinitely at 30—40°. (The *dl*-amide had m. p. 52—53°.)

The Beckmann transformation therefore falls into line with the rearrangements considered in the first part of this paper, in that asymmetry of the migrating group –CHRR' is substantially preserved, thus providing further proof that the reaction is intramolecular.

Retention of Configuration during Intramolecular Changes.—The Hofmann and the Curtius reaction have for some time been regarded as proceeding with retention of configuration on the part of the migrating radical ·Cabc (Wallis and Nagel, *J. Amer. Chem. Soc.*, 1931, **53**, 2787; Braun and Friehmelt, *Ber.*, 1933, **66**, 684), and very recently Archer (*J. Amer.*

Chem. Soc., 1940, **62**, 1872) has pointed out an experimental proof that this is actually true. Scrutiny of the literature provides another proof. Wallis and Nagel (*loc. cit.*) converted (+)benzylmethylacetic acid into the (+)amide and thence into (+)α-benzylethylamine hydrochloride; the same result had been obtained *via* the (+)azide (Jones and Wallis, *ibid.*, 1926, **48**, 169). Now, it has also been established (Kenyon, Phillips, and Pittman, J., 1935, 1072) that (−)benzylmethylacetic acid has the same configuration as (−)α-benzylethylamine hydrochloride [from the (+)amine], each being produced from (+)α-benzylethyl *p*-toluenesulphonate by a series of reactions involving one Walden inversion. Therefore, the (+)α-benzylethylamine obtained from the Hofmann and the Curtius reaction had the same configuration as the original (+)benzylmethylacetamide or azide respectively. It will further be seen from the present work that α-phenylethylamine has the same configuration whether it is obtained through the Hofmann or the Curtius rearrangement.

It may also be noted that Wallis and his co-workers (Wallis and Dripps; Jones and Wallis; *locc. cit.*) obtained *N*-α-benzylethylurea of the same rotatory power and sign of rotation, either by the Curtius rearrangement or by the Lossen rearrangement of the corresponding hydroximic benzoate, starting in each case from the same (+)benzylmethylacetic acid.

Since it may now be presumed that (+)γ-heptylamine and its (−)acetyl derivative have the same configuration as (+)ethylbutylacetic acid and (−)methyl γ-heptyl ketoxime, it follows that the Beckmann rearrangement also does not involve a Walden inversion. Arcus, Balfe, and Kenyon (J., 1938, 485) have previously observed that relative configuration was retained during the intramolecular conversion of (−)phenylmethylcarbinyl *p*-toluenesulphinate into the corresponding sulphone.

Sprung and Wallis (*J. Amer. Chem. Soc.*, 1934, **56**, 1715) have described the rearrangement of (+)phenyl β-butyl ether into (+)*o*-β-butylphenol. This ether has been configurationally related to (+)β-butylbenzene (Kenyon, Phillips, and Pittman, *loc. cit.*), and it is reasonable to assume that (+)*o*-β-butylphenol has the same configuration as (+)β-butylbenzene, leading to the conclusion that in this reaction, too, the migrating radical is transferred without inversion.

The general conclusion is therefore reached that where an optically active radical ·Cabc undergoes transference in an intramolecular change, it retains its configuration as well as its asymmetry.

In the last two rearrangements mentioned, at any rate, the asymmetric carbon atom almost certainly undergoes a replacement of one of its electron pairs during its transfer, so that if the reaction were entirely parallel to the corresponding nucleophilic substitution, an inversion would be expected. Ingold and his collaborators (J., 1937, 1259) have discussed the question briefly without reference to experimental evidence, and concluded that in intramolecular processes of this nature an inversion does not take place where it is rendered difficult or impossible for steric reasons. The observed retention of configuration is therefore an excellent proof that these reactions are truly intramolecular (Hammett, "Physical Organic Chemistry," New York, 1940, p. 327; cf. also Gilbert and Wallis, *J. Org. Chem.*, 1940, **5**, 184).

In rearrangements of the Hofmann and the Beckmann type, the migrating carbon atom can be formulated as carrying its full octet throughout its transference, so that on the analogy of an electrophilic substitution an inversion is not to be expected (cf. Nevell, de Salas, and Wilson, J., 1939, 1188); this view is in harmony with the ease with which these reactions take place, in contrast to the sulphinate and phenyl ether rearrangements which show a strong tendency to proceed by *inter*molecular paths and to lead to by-products.

Experimental.

Conversion of the Azide of (+)*Hydratropic Acid into* (−)α-*Phenylethylamine.*—(i) A mixture of (+)hydratropic acid (5·5 g.) and phosphorus trichloride (2·0 g.) was kept at 60—65° for an hour and then cooled; the upper layer of hydratropoyl chloride was poured into a suspension of sodium azide (10 g., freshly precipitated from its aqueous solution by acetone) in dry ether, and the mixture stirred for 24 hours. The filtered solution had a pronounced odour of *iso*-

cyanate and on gentle warming evolved a steady stream of gas; when the reaction had become slow the ether was removed, and concentrated hydrochloric acid added to the oily residue, whereupon there was a renewed evolution of gas. The mixture was heated at about 50° until the reaction had ceased, diluted with water, and extracted with ether. The amount of recovered hydratropic acid was too small to distil. The hydrochloric acid solution was rendered alkaline and extracted with ether; the dried (sodium hydroxide) and evaporated solution yielded (−)α-phenylethylamine (3 c.c.), b. p. 70°/12 mm., $\alpha_{5461}^{16°}$ − 22·76° (*l*, 0·5), which value is 99·3% of that for the optically pure (−)amine ($\alpha_{5461}^{16·5°}$ − 22·92°; Ingold and Wilson, J., 1933, 1503); acetyl derivative, m. p. 103—104°.

(ii) In a preliminary experiment using (−)hydratropic acid (7·5 g., of $\alpha_{5893}^{18°}$ − 14·96°; *l*, 0·5), where the stirring with sodium azide was not so efficient, there were obtained (+)α-phenylethylamine (3 g.), b. p. 69·5°/12 mm., $\alpha_{5461}^{17°}$ + 6·92° (*l*, 0·5), and unreacted (−)hydratropic acid (3·0 g.).

l(−)*Methyl γ-Heptyl Ketone.* [The *l*-configuration is arbitrarily assigned to (−)ethyl-*n*-butylacetic acid.]—*l*(−)Ethyl-*n*-butylacetic acid of $\alpha_{5461}^{21°}$ − 4·38° (Kenyon and Platt, J., 1939, 633) was converted into its (−)bromide, b. p. 97—98°/15 mm., $n_D^{19°}$ 1·4617, $d_4^{20°}$ 1·1927, by warming with phosphorus tribromide and redistilling the top layer. A small portion of this on treatment with concentrated aqueous ammonia yielded *l*(−)ethyl-*n*-butylacetamide, crystallising from water in fine needles, m. p. 98° (rotatory powers in the table). The dl-*bromide*, prepared similarly, had b. p. 97°/19 mm., $n_D^{18°}$ 1·4612, $d_4^{20°}$ 1·1904 (Found, by hydrolysis: *M*, 210; Br, 38·3. $C_8H_{15}OBr$ requires *M*, 207; Br, 38·6%).

To an ethereal solution of dimethylcadmium (Gilman and Nelson, *loc. cit.*), obtained by treating methylmagnesium bromide (from 1·6 g. of metal) with anhydrous cadmium dibromide (9 g.), was added the (−)ethylbutylacetyl bromide (9 g.). After 2 hours' refluxing and standing overnight, water and a little dilute acid were added, and the product steam-distilled. By extraction of the distillate l(−)*methyl γ-heptyl ketone* was obtained as a colourless mobile liquid with a peculiar sickly smell, b. p. 63—64°/9 mm., $n_D^{15°}$ 1·4228, $d_4^{20°}$ 0·8318, $\alpha_{5461}^{18°}$ − 0·26° (*l*, 0·5) (other rotatory powers in the table). Yield 65%. It did not give good analytical figures (Found: C, 74·4; H, 12·5. $C_9H_{18}O$ requires C, 76·0; H, 12·75%), but this was traced to the formation of a high-boiling product, b. p. 101—104°/5 mm., during distillation. The *dl*-ketone had b. p. 73°/15 mm., 176—179°/760 mm.; $n_D^{15°}$ 1·4223; $d_4^{20°}$ 0·8246.

The corresponding acid chloride was found to react incompletely with dimethylcadmium under the above conditions.

Beckmann Transformation of l(+)*Methyl γ-Heptyl Ketoxime.*—The *l*-ketone (3·3 g.) was boiled under reflux in aqueous-alcoholic solution with hydroxylamine hydrochloride (1·7 g.), sodium acetate (4·3 g.) being added in portions during about ½ hour. On dilution and extraction with ether, the oily l(+)methyl *anti*-γ-heptyl ketoxime was obtained, b. p. 111—113°/12 mm., $n_D^{16°}$ 1·4502, $d_4^{20°}$ 0·8840, $\alpha_{5461}^{21°}$ + 0·39° (*l*, 0·5). It was treated with phosphorus pentachloride (5 g.) in dry ether, and after gentle warming to dissolve all the reagent, the solvent was distilled off. The liquid residue was decomposed by addition of ice, and the washed and dried (sodium sulphate) ethereal extract yielded l(+)*aceto-γ-heptylamide*, which was purified by distillation; it had b. p. 143—145°/15 mm., and solidified to a mass of needles, m. p. 43—44·5°. In alcoholic solution this had the rotations given in the table below (Found: N, 9·0. $C_9H_{19}ON$ requires N, 8·9%).

Table of Specific Rotatory Powers.

Compound.	State.	*t*.	[α]λ. λ=6438.	5893.	5780.	5461.	4358.
l-Ethyl-*n*-butylacetyl bromide	Homog.	20°	−0·30°	−0·36°	−0·39°	−0·44°	−0·97°*
	In Et_2O; *c*, 7·069	20	−0·4	−0·7	−1·1	−1·2	−6·0*
l-Methyl γ-heptyl ketone	Homog. ($d_4^{18°}$ = 0·8399)	18	−0·42	−0·56	−0·57	−0·61	−1·42
	In EtOH; *c*, 5·313	21	−0·5	−0·7	−0·8	−0·9	−1·5
l-Methyl γ-heptyl ketoxime	Homog.*	21	+0·33	+0·38	+0·66	+0·87	+3·41
	In Et_2O; *c*, 5·000	20	+0·1	+0·1	+0·3	+0·3	+1·3
l-Aceto-γ-heptylamide	In EtOH; *c*, 4·001 †	21	+0·9	+1·0	+1·2	+1·4	+5·3
l-Ethyl-*n*-butylacetamide	In EtOH; *c*, 2·340 †	20	−1·3	−2·9	−3·1	−3·9	−6·8

* *l*, 0·5. † *l*, 1·0. All others are *l*, 2.

Synthesis of dl- *and* (−)*Aceto-γ-heptylamide.*—(a) Via *γ-heptylamine. dl*-Ethyl-*n*-butylacetic acid was converted by phosphorus trichloride into its chloride, b. p. 68°/13 mm. (Tiffeneau,

Bull. Soc. chim., 1923, **33**, 185, gives b. p. 85—90°/20 mm.), which on treatment with aqueous ammonia (*d* 0·880) gave the *dl*-amide, short needles (from hot water), m. p. 102° (Raper, J., 1907, **91**, 1837, gives 101—102°). 21 G. of this amide were added to a solution of bromine (8 c.c.) in sodium hydroxide (25 g. in 150 c.c. of water). After ½ hour's warming, dl-*γ-heptylamine* had separated, which after extraction with ether and drying over potassium hydroxide had b. p. 140—142°, $n_D^{19°}$ 1·4224, $d_4^{20°}$ 0·7781 (Found: N, 12·1. $C_7H_{17}N$ requires N, 12·2%); its *hydrochloride* crystallised from ethyl acetate in small needles, m. p. 169—170° (Found: Cl, 23·1. $C_7H_{17}N$,HCl requires Cl, 23·5%). Warming the amine with acetyl chloride and addition of water afforded dl-*aceto-γ-heptylamide*, which was recrystallised, with some difficulty, by dissolving it in a little acetic acid and adding water; it formed needles, m. p. 52—53° (Found: N, 8·2. $C_9H_{19}ON$ requires N, 8·9%).

A partly active (+)ethyl-*n*-butylacetic acid, α_{5893} + 0·53° (*l*, 0·25), was converted by similar methods successively into the (+)chloride, b. p. 86—89°/21 mm., $n_D^{19°}$ 1·4339, $d_4^{21°}$ 0·9468, $\alpha_{5461}^{20°}$ + 0·94° (*l*, 2) (Found: Cl, 21·5; *M*, 165. Calc. for $C_8H_{15}OCl$: Cl, 21·8%; *M*, 163); (+)amide, m. p. 100—101°, $[\alpha]_{4561}^{20°}$ + 0·7° (in alcohol) (not recrystallised); (+)γ-heptylamine, b. p. 140—142°, $n_D^{19°}$ 1·4188, $\alpha_{5461}^{21°}$ + 0·15° (*l*, 0·25); and *d* + *dl*(−)aceto-γ-heptylamide, b. p. 140—145°/15 mm., m. p. 35—45°, $[\alpha]_{5893}^{21°}$ − 0·8, $[\alpha]_{5461}^{21°}$ − 0·6°, $[\alpha]_{4358}^{21°}$ − 2·0° (*c*, 1·969; *l*, 1) in ethyl alcohol.

(b) Via *the Beckmann rearrangement*. The *dl*-ketone yielded an *oxime*, b. p. 113—114°/13 mm., $n_D^{14°}$ 1·4525, $d_4^{25°}$ 0·8822 (Found: N, 8·5. $C_9H_{19}ON$ requires N, 8·9%). Treatment of the oxime (4 g.) in ether with 6 g. of phosphorus pentachloride gave crude *dl*-aceto-γ-heptylamide, m. p. 42—46°, which after three recrystallisations was raised to 50—52° alone or mixed with the product from (a).

The same (+)ethylbutylacetic acid was also converted through its (+)bromide [b. p. 112—113°/24 mm., $n_D^{19°}$ 1·4599, $\alpha_{5461}^{20°}$ + 0·15° (*l*, 2)] into a (+)methyl heptyl ketone, b. p. 71°/13 mm., $n_D^{18°}$ 1·4228, $\alpha_{5461}^{18°}$ + 0·12° (*l*, 2), the *d* + *dl*-oxime [b. p. 116—117°/15 mm., $n_D^{19°}$ 1·4522, $\alpha_{5461}^{20°}$ − 0·05° (*l*, 0·25)] of which was subjected as before to the Beckmann reaction, giving *d* + *dl*(−)aceto-γ-heptylamide, b. p. 148—150°/17 mm., m. p. 30—40°. This had $[\alpha]_{5893}^{21°}$ − 0·7°, $[\alpha]_{5780}^{21°}$ − 0·7°, $[\alpha]_{5461}^{21°}$ − 0·7°, $[\alpha]_{4358}^{21°}$ − 1·2° in alcohol (*c*, 5·046; *l*, 2), and its rotation was also observed in the molten (supercooled) condition: it had $\alpha_{5893}^{20°}$ − 0·48°; $\alpha_{5780}^{20°}$ − 0·53°; $\alpha_{5461}^{20°}$ − 0·62°; $\alpha_{4358}^{20°}$ − 1·00° (*l*, 0·5).

Attempted Resolution of Methyl β-Butyl Ketone.—*o*-Carboxyphenylhydrazine hydrochloride (Heller and Jacobsohn, *Ber.*, 1921, **54**, 1115) was best converted into the base by dissolution in concentrated alkali and acidification with acetic acid at 0°. Warming of equivalent quantities of the base and *dl*-methyl β-butyl ketone in 75% alcohol gave the *hydrazone*, dull yellowish-white, narrow plates from light petroleum (Found: N, 11·8. $C_{13}H_{18}O_2N_2$ requires N, 12·0%). In methyl-alcoholic solution this readily afforded a strychnine salt, m. p. 172—173°, and fractional crystallisation of the latter gave, after decomposition, dextro- and lævo-rotatory hydrazones, having $[\alpha]_{5461}^{18°}$ + 3·3° and − 4·7° respectively. However, further experiments indicated that separation was irregular, apparently depending on the speed of separation of the diastereoisomerides rather than a genuine difference in solubility.

Thanks are due to the Government Grants Committee of the Royal Society and to Imperial Chemical Industries Ltd. for grants, and to the D.S.I.R. for a maintenance grant to one of us (D. P. Y.).

BATTERSEA POLYTECHNIC, LONDON, S.W. 11. [*Received, October 25th*, 1940.]

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47. *The Halogenation of Phenolic Ethers and Anilides. Part X. Substituted Tolyl Ethers.*

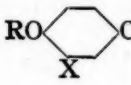
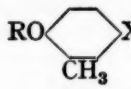
By BRYNMOR JONES.

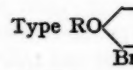
The kinetic study of the chlorination of ethers of the general formula $OR{\cdot}C_6H_4{\cdot}X$ has now been extended to include several series of aromatic ethers which contain, in addition to the group X, one or more methyl substituents. Analysis of the results obtained hitherto in terms of the equation $k = PZe^{-E/RT}$ has shown that the changes in velocity are to be attributed to variations in the energy of activation, and that in ethers of the type p-$OR{\cdot}C_6H_4{\cdot}X$ the groups OR and X each contribute a characteristic quota to the activation energy of further substitution. This has been found to be so when-

ever R is an alkyl, benzyl, or substituted benzyl group and X a deactivating substituent. For six new series of ethers the present results show that, when an activating group such as methyl is also present in the nucleus which undergoes chlorination, the simple additive relationships previously found are not strictly applicable in all cases. The significance of this is discussed.

An earlier kinetic investigation of the chlorination of a few *p*-tolyl ethers of the type (I) revealed a definite tendency to departure from the simple additive relationships for the energies of activation found in several series of ethers of the type *p*-OR·C_6H_4X. As this was the first departure from the additive rule to be observed, it was important to determine whether it was characteristic of all disubstituted ethers or whether the departure from

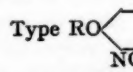
Table I.

Velocity coefficients for the chlorination of substances of the types  *and*  *in 99% acetic acid, at 20°.*

Type  .

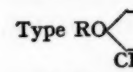
$[Cl_2] = 0.0075$; $[HCl] = 0.0375$. $[Cl_2] = 0.0050$; $[HCl] = 0.0250$.

Concn. of ether	0·0225	0·0375	0·0150
Mol. propn.	3	5	3
Group R.	*k*.		*k*.
CH_3	7·12	—	—
C_2H_5	13·2	—	—
CH_2Ph	3·92	3·77	3·88
p-$C_6H_4Me·CH_2$	5·47	5·18	5·37
p-$C_6H_4Et·CH_2$	5·45	5·21	5·43
p-$C_6H_4Cl·CH_2$	—	—	2·23
p-$C_6H_4Br·CH_2$	2·20	2·10	2·15
p-$C_6H_4(NO_2)·CH_2$	0·807	—	—
m-$C_6H_4F·CH_2$	1·90	—	1·89
m-$C_6H_4(NO_2)·CH_2$	0·936	—	—
o-$C_6H_4Cl·CH_2$	1·56	1·50	1·55
o-$C_6H_4(NO_2)·CH_2$	0·76	—	0·76

Type  .

$[Cl_2] = 0.04$; [ether] = 0·12; [HCl] = 0·05.

Group R	CH_3	C_2H_5	$C_3H_7{}^\beta$	$C_4H_9{}^a$
k	0·022	0·042	0·075	0·046

Type  .

$[Cl_2] = 0.0075$; $[HCl] = 0.0375$.

Concn. of ether	0·0225	0·0075	Concn. of ether	0·0225	0·0075
Mol. propn.	3	1	Mol. propn.	3	1
Group R.	*k*.		Group R.	*k*.	
CH_3	4·36	4·60	*p*-$C_6H_4Bu^\gamma·CH_2$	3·08	—
C_2H_5	8·63	9·04	*p*-$C_6H_4Cl·CH_2$	1·38	1·53
$C_3H_7{}^a$	9·14	9·71	*p*-$C_6H_4Br·CH_2$	1·34	—
$C_3H_7{}^\beta$	14·16	—	*p*-$C_6H_4(NO_2)·CH_2$	—	0·528
$C_5H_{11}{}^a$	9·25	—	*m*-$C_6H_4F·CH_2$	1·09	—
CH_2Ph	2·28	2·52	*m*-$C_6H_4Cl·CH_2$	1·03	—
p-$C_6H_4Me·CH_2$	3·18	3·47	*o*-$C_6H_4Cl·CH_2$	0·915	—
p-$C_6H_4Et·CH_2$	3·18	—	*o*-$C_6H_4(NO_2)·CH_2$	0·383	—

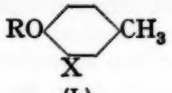
$[Cl_2] = 0.0075$; [ether] = 0·0150; [HCl] = 0·0375.

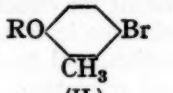
R = CH_2Ph; $k = 2.31$ R = *p*-$C_6H_4(NO_2)·CH_2$; $k = 0.491$

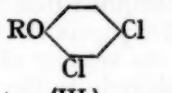
$[Cl_2] = 0.0050$; [ether] = 0·0150; [HCl] = 0·0250.

R = CH_3; $k = 4.35$ R = C_2H_5; $k = 8.56$ R = $C_3H_7{}^a$; $k = 9.08$.

additivity occurs only when activating groups are present in the molecule. The three series of disubstituted ethers investigated have the general formulæ (I), (II), and (III).


(I.)


(II.)

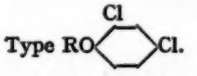
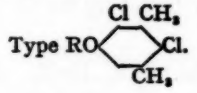
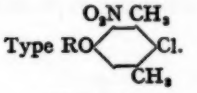

(III.)

Such ethers have the advantage that one position only is available for chlorination, and the velocity coefficients relate to reaction at a single nuclear position. This is true also of the disubstituted ethers of *s.*-*m*-xylenol examined.

The mean values of the bimolecular velocity coefficients now reported are given in Tables I and II. As in earlier papers, the medium is " 99% acetic acid " (1 c.c. of water per 100 c.c. of solution), the concentrations are in g.-mols./l., and the time in minutes. The relative directive powers of the OR groups are again given in the form $100k_X^{OR}/k_X^{OMe}$; $k_{p\text{-}X}^{OR}$ represents the velocity coefficient for the chlorination of *p*-OR·C_6H_4X.

TABLE II.

Velocity coefficients of chlorination in 99% *acetic acid, at* 20°.

	Type 	Type 		Type 
	$[Cl_2] = 0{\cdot}04$; $[HCl] = 0{\cdot}0475$.	$[Cl_2] = 0{\cdot}0075$; $[HCl] = 0{\cdot}0375$.		$[Cl_2] = 0{\cdot}02$; $[HCl] = 0{\cdot}0475$.
Concn. of ether	0·12	0·0225	0·0075	0·04
Mol. propn.	3	3	1	2
	k.	*k*.		*k*.
R = CH_3	0·00321	14·1	14·5	0·0386
C_2H_5	0·00641	—	27·0	0·0690
C_3H_7[a]	0·00697	—	28·3	0·0748
C_6H_{13}[a]	—	—	—	—
CH_2Ph	0·00223	8·05	8·16	0·0728
p-$C_6H_4Cl{\cdot}CH_2$	—	4·89	—	—
p-$C_6H_4Br{\cdot}CH_2$	—	4·71	—	—
m-$C_6H_4F{\cdot}CH_2$	—	3·85	—	—
m-$C_6H_4Cl{\cdot}CH_2$	0·0010	3·75	—	—
o-$C_6H_4Cl{\cdot}CH_2$	—	3·20	—	—

DISCUSSION.

The current practice, first introduced by Bradfield and Jones (J., 1928, 1006), of analysing data relating to reaction rates in solution in terms of the equation $k = PZe^{-E/RT}$ has led to a clearer understanding of the way in which constitutional changes affect chemical reactivity by focusing attention on the fact that the changes in velocity may be due to variations in *P*, in *E*, or in both *P* and *E*. Among the several reactions studied, two main groups can be distinguished: (1) reactions in which the differences in velocity can be accounted for, almost entirely at least, by variations in the energy of activation, changes in the value of *P* in comparison being almost negligible; (2) reactions in which simultaneous variations in *E* and in *P* are found. Characteristic of these two groups of reactions is the circumstance that, in the first, the variable substituent is well removed from the point of reaction, when disturbances of a local nature are reduced to a minimum, while in the second group the variable substituent is usually near to the reactive centre (for references, cf. Watson, *Ann. Reports*, 1938, **35**, 236).

The nuclear chlorination of phenolic ethers of the general type *p*-OR·C_6H_4X has been shown to be a reaction of the first type. Although the nature of the reactants and of the medium imposes severe limitations on the temperature range over which measurements can be made, yet a careful study of the velocity coefficients of closely related series of ethers over a range of 15° has shown that, to the degree of exactness that can be expected over this limited range, *P* is constant. Small changes in *P* are not unexpected, but for

ethers of the above type these are only of minor importance and the differences in reaction rates are attributed, mainly at least, to variations in the energy of activation.

On the assumption that P is constant for closely related series of ethers, it has been shown in earlier papers (1) that variations in E alone are sufficient to account for the differences in the velocity of chlorination, and (2) that the two substituents OR and X contribute additively to the energy of activation. This relationship has been found to hold for several series of ethers of the above type where X is a deactivating halogen atom (F, Cl, or Br) or a meta-directing group such as NO_2, CO_2H, COPh, or SO_2Ph.

The possibility of an extension of this limited generalisation was naturally visualised at the outset, and several new series of ethers which contain activating as well as deactivating substituents in the nucleus which undergoes substitution have been investigated.

In the chlorination of ethers of the types (I, X = Br), (II), and (III) the critical energy increment relating to the single point of entry will presumably be governed by the influence of all three substituents; *i.e.*, for the tolyl ethers, $E = E_0 + E_{OR} + E_{CH_3} + E_{Br}$, where E_0 is the critical increment in the unsubstituted compound, E_{OR} the energy contribution of the group OR to the point of attack, and E_{CH_3} and E_{Br} the modifying influence of the substituents CH_3 and Br.

Consequently, by analogy with the expressions developed in previous papers the following expression may be set up for (I, X = Br):

$$k(\text{obs.}) = k\begin{cases}\text{OR (4)}\\ \text{Br (3)}\\ \text{CH}_3\text{ (1)}\end{cases} = PZe^{-(E_0 + E_{OR} + E_{Br} + E_{CH_3})/RT}$$

and a similar expression obtains when R′ is substituted for R in this ether. If the small variations due to differences in molecular weight are neglected, and as in the earlier papers P is assumed to be constant for a closely related series of ethers, then

$$k\begin{cases}\text{OR′ (4)}\\ \text{Br (3)}\\ \text{CH}_3\text{ (1)}\end{cases} \Big/ k\begin{cases}\text{OR (4)}\\ \text{Br (3)}\\ \text{CH}_3\text{ (1)}\end{cases} = e^{(E_{OR} - E_{OR'})/RT}$$

Further, change of the alkyl group R to R′ in the series (II) and (III) leads to an identical expression; *i.e.*, in all three series the same expression is obtained as for the simpler ethers of the type *p*-OR·C_6H_4X.

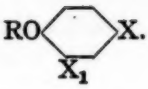
From this result two conclusions follow: (1) the relative directive powers of the OR groups in the three series of ethers should be independent of the nature of the other substituents present in the nucleus, and, in the tolyl ethers, of the actual positions of the methyl and bromine substituents; (2) the velocity ratios for the three series should be the same as those already found for the simple *p*-substituted phenyl ethers.

Examination of the velocity ratios given in Table III shows that these expectations, based on the assumption of the constancy of P, are only partly realised and the following points emerge: (1) In the tolyl ethers the relative directive powers of OR groups are found to be independent of the actual positions in the nucleus of the methyl and bromine substituents; (2) in the 2 : 4-dichlorophenyl ethers only are the same velocity ratios observed as in the ethers of the type *p*-OR·C_6H_4X. In both series of tolyl ethers they differ by approximately 15%, showing that the relative directive powers of the OR groups are not independent of the polar nature of the other groups present in the benzene nucleus.

This modification of the relative directive powers of OR groups as a result of the introduction of a methyl group into the nucleus which undergoes substitution occurs also in other series of ethers. Thus the presence of two methyl groups in 2 : 4-dichloro-3 : 5-dimethyl phenyl ethers modifies the velocity ratios found for the 2 : 4-dichlorophenyl ethers so that they no longer correspond with those for the monosubstituted ethers but instead show good agreement with the values obtaining in the tolyl series.

This effect of methyl groups is thus seen to be quite regular. At present its explanation can be approached only in a tentative way. Recent studies of reaction kinetics by Hinshelwood, Watson, and others (cf. Hinshelwood and Legard, J., 1935, 587; Hinshelwood and Winkler, J., 1936, 371; Watson, *Ann. Reports*, 1938, **35**, 238) have shown that, when the

TABLE III.

Relative directive powers of the groups OR *in compounds of the type* 

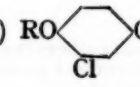
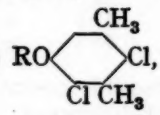
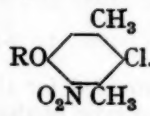
Values of $100k^{OR}_{XX_1}/k^{OMe}_{XX_1}$.

	R = CH_3.	C_2H_5.	$C_3H_7\alpha$.	$C_3H_7\beta$.	$C_4H_9\alpha$.	$C_5H_{11}\alpha$.
X = CH_3, X_1 = Br	100	185	—	—	—	—
,, X_1 = NO_2	100	195	—	348	211	—
X = Br, X_1 = CH_3	100	197	210	325	—	212
X = Cl, X_1 = Cl	100	199	217	—	—	—
Phenyl ethers (mean)	100	199	223	440	223	221

R = $C_6H_4A{\cdot}CH_3$.

	A = H.	*p*-Me.	*p*-Et.	*p*-Buγ.	*p*-Cl.	*p*-Br.	*p*-NO_2.	*m*-F.	*m*-Cl.	*m*-NO_2.	*o*-Cl.
X = CH_3, X_1 = Br	55	77	77	—	—	31	11·3	27	—	13	22
X = Br, X_1 = CH_3	54	74	73	71	33	31	11·5	25	24	—	21
X = Cl, X_1 = Cl	69	—	—	—	—	—	—	—	32	—	—
Phenyl ethers (mean)	68	95	95	95	42	41	14·1	34	33	16	28

TABLE IV.

Relative directive powers of the groups OR *in compounds of the type* (*a*)  , (*b*)  , (*c*)  .

Values of $100k^{OR}_{X}/k^{OMe}_{X}$.

	R = CH_3.	C_2H_5.	$C_3H_7\alpha$.	$C_6H_{13}\alpha$.	A = H.	*p*-Cl.	*p*-Br.	*m*-F.	*m*-Cl.	*o*-Cl.
Series (*a*)	100	199	217	—	69	—	—	—	32	—
,, (*b*)	100	185	195	—	57	35	34	27	27	23
,, (*c*)	100	179	194	189	—	—	—	—	—	—
Phenyl ethers (mean)	100	199	223	221	68	42	41	34	33	28
Tolyl ethers (mean)	100	192	210	—	55	33	31	26	24	22

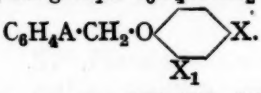
variable group is comparatively near to the point of reaction, the changes in velocity are in many cases to be attributed very largely to variations in *E* but that the factor *P* also undergoes appreciable changes. A somewhat similar state of affairs may occur when methyl groups are present in the above ethers. The presence of a group such as methyl, which raises the general reactivity of the nucleus to which it is attached, at no great distance from other groups or from the point of reaction may possibly cause larger variations in *P* than occur in compounds of the simpler type *p*-OR·C_6H_4X and also, perhaps, some departure from the additive energy relationships. These may result from direct interaction of some kind with other groups and by other "local disturbances." It is noteworthy that the variations from the expected velocity ratios are found mainly when the group R which is varied is a simple alkyl group (cf. Tables III and IV).

When, on the other hand, comparison is restricted to the substituted benzyl ethers, where the variable substituent is in the *m*- or the *p*-position of the aromatic nucleus and therefore at some distance from the reactive centre, then all three series phenyl, tolyl, and xylyl give velocity ratios which show satisfactory agreement. This suggests that for substituted benzyl ethers the conclusions drawn in earlier papers from the study of phenyl ethers apply also to the tolyl and xylyl ethers.

It is significant in this connexion that, when a strongly polar substituent such as a nitro-group is situated in the ortho-position of the benzyl group, differences in velocity ratios appear. The relative directive power of the *o*-nitrobenzyloxy-group in the 3-bromo-*p*-tolyl series is 19·5 and in the isomeric 5-bromo-*o*-tolyl series 16·8, whereas the mean value found in the simple phenyl ethers is 21.

TABLE V.

Relative directive powers of the groups $C_6H_4A\cdot CH_2\cdot O$ *in compounds of the type*

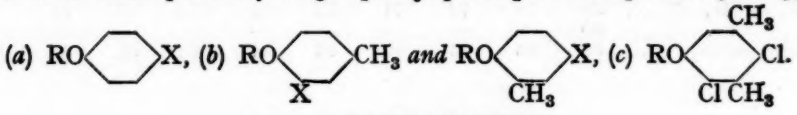


Values of $100k_{XX_1}^{O\cdot CH_2\cdot C_6H_4A}/k_{XX_1}^{O\cdot CH_2Ph}$.

	A = H.	*p*-Me.	*p*-Et.	*p*-Bu$^{\gamma}$.	*p*-Cl.	*p*-Br.	*p*-NO_2.	*m*-F.	*m*-Cl.	*m*-NO_2.	*o*-Cl.
X = CH_3, X_1 = Br	100	138	139	—	58	56	21	49	—	24	40
X = Br, X_1 = CH_3	100	139	139	135	61	59	21	48	45	—	40
Phenyl ethers (mean)	100	139	139	139	60	58	21	49	47	24	41

TABLE VI.

Relative directive powers of the groups $C_6H_4A\cdot CH_2\cdot O$ *in compounds of the type*



Values of $100k_{X}^{O\cdot CH_2\cdot C_6H_4A}/k_{X}^{O\cdot CH_2Ph}$.

	A = H.	*p*-Cl.	*p*-Bγ.	*p*-NO_2.	*m*-F.	*m*-Cl.	*o*-Cl.
(*a*) Phenyl ethers (mean)	100	60	58	21	49	47	41
(*b*) Tolyl ethers (mean)	100	59·5	57·5	21	48·5	45	40
(*c*) Xylyl ethers	100	61	58·5	—	48	46·5	40

In view of the scope provided for the possible operation of complicating factors in polysubstituted ethers of the type of the 2 : 4-dichloro-3 : 5-dimethylphenyl ethers it is a matter of particular interest that the relative directive powers of OR groups observed in this series differ by only 15% from those found in the simpler ethers of the type *p*-OR·C_6H_4X.

A more complete understanding of the influence of nuclear-situated methyl groups in these several series requires the determination of velocity coefficients over as wide a range of temperature as possible and the analysis of these in terms of the two parameters of the Arrhenius equation.

Two interesting examples of the well-known effect of methyl in raising the general level of reactivity of the nucleus to which it is attached are provided by the comparison of the velocity coefficients for the two pairs of ethers (*a*) *p*-bromophenyl ethers and the 5-bromo-*o*-tolyl ethers, and (*b*) the 2 : 4-dichlorophenyl and the corresponding 2 : 4-dichloro-3 : 5-dimethylphenyl ethers. The presence of a single methyl group in the 5-bromo-*o*-tolyl ethers increases the rate of chlorination as compared with the *p*-bromophenyl ethers 2·7 times although there is only one of the two ortho-positions free for substitution. In the second pair the effect is more striking, for the introduction of two methyl groups into the 2 : 4-dichlorophenyl ethers increases the velocity of chlorination over 4000 times.

The ethers investigated in this series of papers are now sufficiently varied to make it possible, by employing the above velocity ratios, to predict the actual velocity of chlorination of individual ethers under standard conditions provided the velocity coefficient of one member of the series be known accurately.

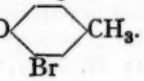
The main conclusions of this investigation may be summarised as follows: (1) For a series of 2 : 4-dichlorophenyl ethers the same relative directive powers of OR groups are found as for the simpler ethers of the type *p*-OR·C_6H_4X investigated in earlier papers. (2) When a methyl group is present in the nucleus which undergoes substitution, as in the tolyl ethers, or when two methyl groups are present as in the 2 : 4-dichloro-3 : 5-dimethylphenyl ethers, there is a divergence of approximately 15% from the mean values found for the monosubstituted phenyl ethers. When, however, comparison is restricted to a range of substituted benzyloxy-groups where the variable substituent is situated in the *m*- or *p*-positions of the aromatic nucleus and is therefore well removed from the point of reaction, the same velocity ratios are observed in the phenyl, tolyl, and xylyl series. (3) The

discovery for polysubstituted compounds such as the 2 : 4-dichloro-3 : 5-dimethylphenyl ethers of relative directive powers of OR groups which differ so little from the values obtaining in the simple monosubstituted ethers is a significant feature of the present work. (4) Comparison of the velocity coefficients of analogous 2 : 4-dichlorophenyl and 2 : 4-dichloro-3 : 5-dimethylphenyl ethers shows that the presence of the two methyl groups increases the rate of chlorination more than 4000 times.

Experimental.

Velocity Measurements.—The method of determining the velocity coefficients was the same as in the author's previous work and satisfactory values were obtained in all cases. With the 3-bromo-*p*-tolyl ethers, however, it was reported in Part III, and now confirmed, that when measurements are made with equal initial concentrations of reactants the velocity coefficients show a steady rise of approximately 10%. When, on the other hand, the molecular ratio of ether to chlorine is increased to 3 : 1, the drift in the values of the velocity coefficients is no longer detectable and satisfactory constants are obtained. Nevertheless, the existence of a secondary reaction of this magnitude makes the figures recorded in Table I for this series of ethers a little less trustworthy than those given for other series, but so far as the relative directive powers of groups are concerned, it is clear from Table VII that the above discrepancy has no noticeable effect, since ratios of velocity coefficients remain unaltered by a further increase in the ether : chlorine ratio to 5 : 1.

Table VII.

Effect of relative concentrations of ether to chlorine on the directive powers of the groups $C_6H_4A\cdot CH_2\cdot O\cdot$ *in ethers of the type* 

Values of $100k_X^{O\cdot CH_2\cdot C_6H_4A}/k_X^{O\cdot CH_2Ph}$.

Mol. propn. ether : chlorine.	A = H.	*p*-Me.	*p*-Et.	*p*-Cl.	*p*-Br.	*p*-NO_2.	*m*-F.	*m*-NO_2.	*o*-Cl.
3 : 1	100	139	139	—	56	21	49	24	40
5 : 1	100	137	138	—	56	—	—	—	40
3 : 1	100	138	140	58	55	—	49	—	40

The cause of the upward drift in the velocity coefficients is not clear, but it is significant that the isomeric 5-bromo-*o*-tolyl ethers give satisfactory constants at all concentrations. This suggests that, when it is in the *p*-position, the methyl group is itself attacked by chlorine—a view which is supported by the similar behaviour of ethers which have an ethyl or a *n*-propyl group, but not a *tert.*-butyl or -amyl group, in the *p*-position.

To ensure the purity of the specimens used in the velocity measurements, each ether was crystallised three times, usually from ethyl alcohol or glacial acetic acid, and only in exceptional cases was further purification essential. The following random selection of examples illustrates the constancy of the mean values of the velocity coefficients in individual experiments. (1) 5-Bromo-*o*-tolyl benzyl ether had k = 2·27, 2·29, 2·28, and 2·26 after three crystallisations from ethyl alcohol and one from glacial acetic acid, and k = 2·30 after a further crystallisation from benzene. (2) 2 : 4-Dichloro-3 : 5-dimethylphenyl *m*-chlorobenzyl ether, after two crystallisations from ethyl alcohol and one from glacial acetic acid, had k = 3·74, and after two further crystallisations from ethyl alcohol k = 3·76.

Materials.—The ethers were prepared by standard methods from the parent phenol and the appropriate benzyl chloride or bromide, the latter being themselves obtained according to the instructions given in Part IX and J., 1935, 1815.

3-Bromo-*p*-cresol was obtained by bromination of a commercially pure sample of *p*-cresol in ice-cold carbon tetrachloride, and the fraction of b. p. 214—216° employed for the preparation of the 3-bromo-*p*-tolyl ethers. The methyl and ethyl ethers had b. p.'s of 125°/20 mm. and 133°/24 mm. respectively, and the benzyl ether crystallises from alcohol in clusters of colourless prisms, m. p. 43·5° (Found :* C, 60·8; H, 4·9. Calc. : C, 60·6; H, 4·7%). The p-*methylbenzyl* and p-*ethylbenzyl ethers* crystallise from glacial acetic acid in colourless elongated prisms, m. p. 92° (Found : C, 62·1; H, 5·2. $C_{15}H_{15}OBr$ requires C, 61·9; H, 5·2%), and m. p. 67° (Found : C, 63·1; H, 5·7. $C_{16}H_{17}OBr$ requires C, 63·0; H, 5·6%), respectively. The p-*chloro*- and the p-*bromo-benzyl ethers*, the latter obtained from purified *p*-bromobenzyl bromide (cf. J., 1935, 1815), also crystallise from glacial acetic acid in clusters of colourless elongated

* All micro-determinations by Dr. Ing A. Schoeller.

prisms, m. p. 67° (Found: C, 53·9; H, 4·1. $C_{14}H_{12}OClBr$ requires C, 54·0; H, 3·9%), and m. p. 85° (Found: C, 47·2; H, 3·4. $C_{14}H_{12}OBr_2$ requires C, 47·2; H, 3·4%), respectively. From glacial acetic acid the p-*nitrobenzyl ether* crystallises well in long, pale yellow prisms, m. p. 135° (Found: C, 52·2; H, 3·95. $C_{14}H_{12}O_3NBr$ requires C, 52·2; H, 3·8%), and the m-*fluorobenzyl ether* separates from alcohol in large clusters of colourless prisms, m. p. 41° (Found: C, 56·95; H, 4·2. $C_{14}H_{12}OFBr$ requires C, 56·95; H, 4·1%). The o-*chlorobenzyl ether* melts at 54·5° and crystallises from glacial acetic acid in clusters of elongated prisms (Found: C, 54·1; H, 4·1%). The o-*nitrobenzyl ether* crystallises similarly, and after four crystallisations from glacial acetic acid had m. p. 110° (Found: C, 52·9; H, 3·5%).

3-*Nitro*-p-*tolyl ethers*. The methyl, ethyl, *iso*propyl, and *p*-methylbenzyl ethers were prepared from a purchased specimen of *m*-nitro-*p*-cresol, and the butyl and benzyl ethers from a specimen prepared by the nitration of *p*-cresol in glacial acetic acid. The first two ethers were obtained in good yield by the action of the alkyl sulphate on a warm solution of the nitrocresol in sodium hydroxide. The other four were prepared from the appropriate benzyl chloride or alkyl bromide and the nitrocresol in an alcoholic solution of sodium ethoxide. The specimens used for the velocity measurements had the following constants: methyl ether, b. p. 149—150°/13 mm.; ethyl ether, b. p. 151°/13 mm.; *iso*propyl ether, b. p. 175°/33 mm.; *n*-butyl ether, b. p. 172°/13 mm. The benzyl ether melts at 55° and crystallises from alcohol in clusters of colourless prisms, and the p-*methylbenzyl ether* crystallises in pale yellow prisms, m. p. 69° (Found: C, 70·3; H, 5·9. $C_{15}H_{15}O_3N$ requires C, 70·0; H, 5·9%).

5-Bromo-*o*-cresol, prepared by bromination of *o*-cresol in ice-cold carbon tetrachloride and crystallised from ligroin (b. p. 40—60°), had m. p. 62—64°. Five alkyl ethers prepared from this specimen had the following constants: the methyl ether had m. p. 67° and crystallised from ethyl alcohol in flat, colourless plates; the ethyl ether, b. p. 127°/19 mm.; *n*-propyl ether, b. p. 142°/20 mm.; iso*propyl ether*, b. p. 129°/19 mm. (Found: C, 52·8; H, 5·9. $C_{10}H_{13}OBr$ requires C, 52·4; H, 5·7%); the n-*amyl ether*, b. p. 166°/17 mm. (Found: C, 56·6; H, 6·7. $C_{12}H_{17}OBr$ requires C, 56·0; H, 6·7%). The benzyl ether and ten substituted benzyl ethers were also prepared, but even after the usual precautions to ensure pure specimens had been observed the velocity coefficients obtained in individual experiments showed a slight downward drift. This was probably due to the presence in the 5-bromo-*o*-cresol of a small percentage of the unreactive 3 : 5-dibromo-*o*-cresol which was difficult to remove. The ethers were therefore purified until constant values of k were obtained, and in several instances this necessitated five or six crystallisations. The *benzyl ether*, after three crystallisations from ethyl alcohol and two from glacial acetic acid, from which it crystallises in clusters of colourless prisms, melts at 62° (Found: C, 60·9; H, 4·65. $C_{14}H_{13}OBr$ requires C, 60·6; H, 4·7%). The p-*methylbenzyl ether* separates in colourless, elongated prisms, m. p. 83°, after three crystallisations from alcohol and three from glacial acetic acid (Found: C, 61·6; H, 5·1. $C_{15}H_{15}OBr$ requires C, 61·8; H, 5·2%), and the p-*ethylbenzyl ether*, after similar treatment, crystallises in stout, colourless prisms, m. p. 81° (Found: C, 63·0; H, 5·7. $C_{16}H_{17}OBr$ requires C, 63·0; H, 5·6%). The p-tert.-*butylbenzyl ether*, prepared from a pure specimen of *p-tert.*-butylbenzyl bromide, was crystallised in turn from alcohol, twice from benzene, once from glacial acetic acid, and finally from alcohol and had m. p. 99°. It crystallises from ethyl acetate in colourless, monoclinic prisms (Found: C, 64·9; H, 6·5. $C_{18}H_{21}OBr$ requires C, 64·9; H, 6·4%). The p-*chlorobenzyl ether*, after two crystallisations from alcohol and two from glacial acetic acid, separates from the latter solvent in colourless, matted clusters, m. p. 96° (Found: C, 54·2; H, 3·8%). In the preparation of the analogous p-*bromobenzyl ether*, purified *p*-bromobenzyl bromide was used, and the ether, after three crystallisations from glacial acetic acid in which it is not appreciably soluble at room temperature and from which it crystallises in colourless prisms, had m. p. 117° (Found: C, 47·3; H, 3·4%). The p-*nitrobenzyl ether* crystallises from glacial acetic acid in long, pale yellow prisms, m. p. 156° (Found: C, 52·4; H, 3·8%). Its maximum solubility in glacial acetic acid is 0·5 g./100 c.c. at 20°.

The m-*fluorobenzyl* and the m-*chlorobenzyl ethers*, m. p. 73° (Found: C, 57·1; H, 4·1%), and m. p. 63° (Found: C, 53·9; H, 3·95%), respectively, after three crystallisations from glacial acetic acid, separate in colourless elongated prisms. The m-*nitrobenzyl ether*, which crystallises from glacial acetic acid in pale yellow, elongated prisms, m. p. 98°, is sensitive to light, the colour changing gradually to dark brown.

The o-*chlorobenzyl ether* crystallises from glacial acetic acid in clusters of colourless, slender prisms, m. p. 50° (Found: C, 53·9; H, 3·8%), and the o-*nitrobenzyl ether* separates from the same solvent in colourless, long, narrow prisms, m. p. 109°, which darken a little on exposure to diffused light and on melting (Found: C, 52·65; H, 3·7%).

2 : 4-*Dichlorophenyl ethers.* The methyl ether, m. p. 28—29°, the ethyl ether, b. p. 120°/8 mm. (after standing for several years this specimen solidified, m. p. 30—31°), and the benzyl ether, which crystallises from alcohol in clusters of colourless cubes, m. p. 63° (Found : C, 62·1; H, 3·9. Calc. : C, 61·7, H, 4·0%), were prepared from a specimen of 2 : 4-dichlorophenol obtained from *p*-chlorophenol by Orton and King's method of chlorination (J., 1911, **99**, 1185). In the preparation of the other ethers of this series a commercially pure sample of the dichlorophenol was used.

The *n*-propyl ether distils as a colourless liquid, b. p. 127°/13 mm., and the *iso*propyl ether at 118°/13 mm. The p-*methylbenzyl ether* separates from alcohol in clusters of colourless, elongated prisms, m. p. 92° (Found : C, 63·1; H, 4·8. $C_{14}H_{12}OCl_2$ requires C, 62·9, H, 4·5%). From alcohol the m-*chlorobenzyl ether* separates in clusters of colourless, slender prisms, m. p. 51° (Found : C, 54·35; H, 3·15. $C_{13}H_9OCl_3$ requires C, 54·3; H, 3·15%), and the o-*chlorobenzyl ether* crystallises in clusters of elongated prisms, m. p. 65° (Found : C, 54·3; H, 3·05%).

2 : 4-Dichloro-3 : 5-dimethylphenol was obtained from a purchased specimen of 2-chloro-5-*m*-xylenol by Orton and King's method of chlorination, freshly-prepared chloroacetamide being used as the source of chlorine. When the reaction was complete the acetamide was removed by treatment with water and the 2 : 4-dichloro-3 : 5-dimethylphenol, after being dried and crystallised from ligroin, had m. p. 83°. From this the following thirteen ethers were prepared.

The *methyl ether* crystallises from ethyl alcohol in colourless prisms, m. p. 82° (Found : C, 52·65; H, 4·85. $C_9H_{10}OCl_2$ requires C, 52·65; H, 4·9%). The *ethyl*, n-*propyl*, and *octyl ethers* crystallise from alcohol in clusters of elongated prisms : ethyl ether, m. p. 53° (Found : C, 54·85; H, 5·4. $C_{10}H_{12}OCl_2$ requires C, 54·8; H, 5·5%); *n*-propyl ether, m. p. 31° (Found : C, 56·7; H, 6·0. $C_{11}H_{14}OCl_2$ requires C, 56·65; H, 6·0%); octyl ether, m. p. 35° (Found : C, 63·3; H, 7·8. $C_{16}H_{24}OCl_2$ requires C, 63·35; H, 8·0%).

The *benzyl ether* after three crystallisations from ethyl alcohol, from which it separates in colourless prisms, melts at 89° (Found : C, 64·0; H, 4·8. $C_{15}H_{14}OCl_2$ requires C, 64·1; H, 5·0%). The p-*methylbenzyl ether* crystallises similarly and melts at 74° (Found : C, 64·4; H, 5·4. $C_{16}H_{16}OCl_2$ requires C, 65·1, H, 5·5%). The p-*chloro*- and p-*bromo-benzyl ethers* crystallise in colourless, elongated prisms, m. p. 99° (Found : C, 57·0; H, 3·95. $C_{15}H_{13}OCl_3$ requires C, 57·0; H, 4·15%), and m. p. 110° (Found : C, 50·2; H, 3·7. $C_{15}H_{13}OCl_2Br$ requires C, 50·0; H, 3·6%), respectively. Both the m-*fluoro*- and the m-*chloro-benzyl ether* crystallise from ethyl alcohol in colourless, elongated prisms of m. p. 88° (Found : C, 60·4, H, 4·4. $C_{15}H_{13}OFCl_2$ requires C, 60·2; H, 4·4% Found : C, 56·5; H, 4·2%, respectively). The o-*chloro*-isomeride separates from glacial acetic acid in very slender, colourless prisms, m. p. 101° (Found : C, 57·1; H, 4·1%). The p-*nitrobenzyl ether* crystallises from glacial acetic acid in white, elongated prisms, m. p. 157° (Found : C, 55·3; H, 4·3. $C_{15}H_{13}O_3NCl_2$ requires C, 55·2; H, 4·0%), and the m-*isomeride* separates in pale yellow elongated prisms of m. p. 163° (Found : C, 55·5; H, 4·1%). Both these ethers have a low solubility in cold glacial acetic acid : that of the *m*-isomeride is less than 0·25 g./100 c.c. at 20°.

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48. *The Distribution of Nicotine between Trichloroethylene and Water.*

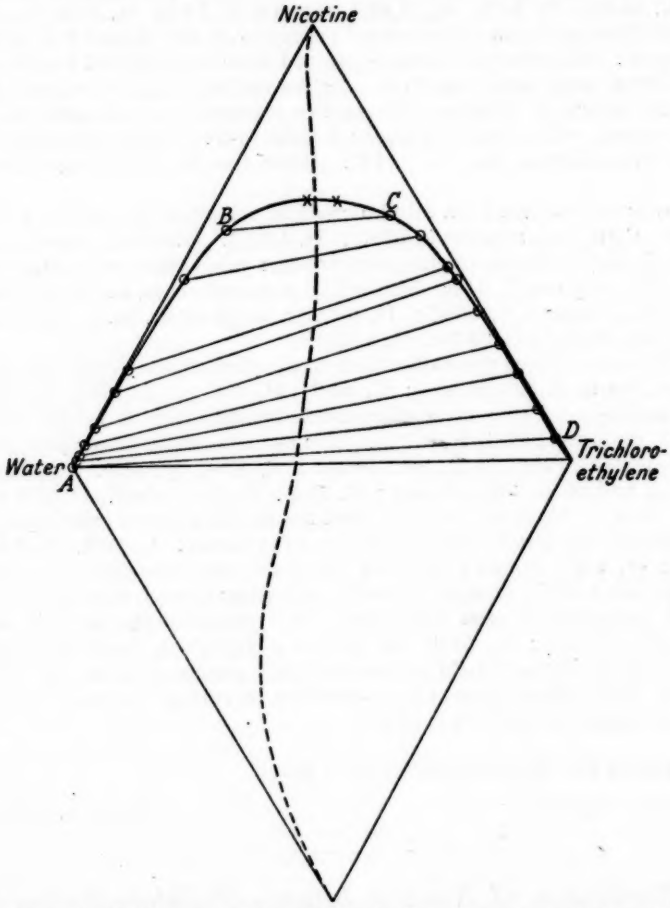
By J. REILLY, D. F. KELLY, and (MISS) M. O'CONNOR.

The distribution of nicotine between trichloroethylene and water has been investigated. The equilibrium curve is also drawn. A " cloud-point " method was employed to complete the construction of the equilibrium curve. A method for the quantitative estimation of trichloroethylene is recorded.

TRICHLOROETHYLENE is completely miscible with nicotine but practically immiscible with water. When nicotine is distributed between trichloroethylene and water (below 61°, the limit of complete miscibility of nicotine and water), the system constitutes a typical three-component system containing two liquid phases.

It was considered that trichloroethylene could be employed to extract nicotine especially

from dilute aqueous solutions, such as would be obtained in the steam distillation of nicotine-containing material. Although the distribution of nicotine between water and various organic solvents has been recorded (*e.g.*, Leone, *Atti Congr. Naz. Chim.*, 1926, pp. 1209—1220; Kolosovskii and Kulikov, *Acta Univ. Central Asia*, 1935, No. 8), the system nicotine–trichloroethylene–water has not hitherto been studied. In the present work the distribution of the three components in equilibrium at some fixed temperatures has been investigated. A method has also been evolved for the quantitative estimation of trichloroethylene. In the distribution experiments the concentrations of nicotine and trichloroethylene in the " water " layer and of water in the " trichloroethylene " layer were determined directly. The remaining concentrations were calculated by difference. For 17°, the



distribution is shown in the figure. The conjugate line fixes the position of the plait-point. The smoothness of this line is noteworthy. With the change in the direction of the tie-lines, the plait-point occurs at about the summit of the equilibrium curve. There appear to be but relatively few cases of three-component systems with the plait-point at the summit of the equilibrium curve.

At 17° nicotine is completely miscible with either trichloroethylene or water, and these two solvents are regarded as being practically immiscible, for at 18° trichloroethylene dissolves 0·0250% (by wt.) of water, and at 16° the solubility of trichloroethylene in water is 0·081% (by wt.). The results plotted on the triangular diagram (cf. also table, p. 277) show, as expected, that, as the percentage of nicotine in the system increases, the mutual solubilities of the two solvents also increase: the water in the trichloroethylene layer increases from 0·66 to 6·81% as the total nicotine content of the system increases from

1·54 to 54·18%, but the trichloroethylene in the water layer increases only from 0·10 to 3·84% over the same range of nicotine concentration. The variation of the distribution ratio α (cf. table, below) with increase in nicotine concentration shows a falling away towards unity at the plait-point of the binodal curve. Further, from the point of view of extracting nicotine with trichloroethylene from dilute aqueous solutions, the high values of α at low concentrations of nicotine are of importance, as also is the small loss of trichloroethylene (due to its low solubility in the water layer). A relatively small number of washings of dilute aqueous nicotine solutions with trichloroethylene should suffice, in practical application, to extract the greater portion of the alkaloid. The separation of even relatively concentrated solutions of nicotine and trichloroethylene by fractional distillation should offer no difficulty owing to the widely different vapour pressures of the substances.

In practice, the extraction of nicotine from aqueous solution with trichloroethylene would be effected at room temperature, so the equilibrium data for 17° are of most interest. The application of a " cloud-point " method gave, for purposes of comparison, equilibrium curves (without tie-lines) for other temperatures. Such curves have shown that with increase in temperature there is a rise of nicotine content in what would be expected to be the plait-point mixtures.

Experimental.

The nicotine used was " Kahlbaum, specially purified "; by the silicotungstic acid method, it was found to contain 99·5—99·7% of nicotine. It had $d_4^{17°}$ 1·018. Trichloroethylene, specially purified and free from " stabilisers," was obtained from Imperial Chemical Industries, Ltd. Distilled water free from basic substances was employed.

Measured amounts of nicotine, trichloroethylene, and water were shaken vigorously in a separating funnel and kept at 17°. The layers were separated, and their compositions ascertained by analysis, nicotine being determined by addition of excess of standard hydrochloric acid solution, followed by the titration of the excess with standard sodium hydroxide solution, cochineal being the indicator (Young, *Analyst*, 1927, **52**, 15) (1 c.c. of 0·1N-acid = 0·0162 g. of nicotine). The water present in the trichloroethylene layer was estimated by the magnesium nitride method (Dietrich and Conrad, *Z. angew. Chem.*, 1931, **44**, 532), the ammonia evolved in the reaction $Mg_3N_2 + 6H_2O = 3Mg(OH)_2 + 2NH_3$ being determined by absorption in standard sulphuric acid; Kahlbaum's magnesium nitride, specially prepared for the process, was used. The portion of the trichloroethylene layer in which the water was to be estimated was allowed to flow slowly from a funnel into a flask containing the nitride. The funnel was then washed with anhydrous propyl alcohol, followed by anhydrous light petroleum—preliminary use of the former solvent having been found to lead to more accurate results. The flask was heated slowly on a wire gauze until about half of its contents had distilled. It was found unnecessary to " fix " the nicotine in the distilling flask with anhydrous tartaric acid.

No chemical method has been published for the determination of trichloroethylene, but its quantitative hydrolysis was found to be suitable. Under ordinary pressure, hydrolysis by aqueous potassium hydroxide solution is not quantitative, but at higher pressures potassium chloride is formed in amount equivalent to the total chlorine present, so reaction was carried out for 3 hours at 150° in a sealed Carius tube; the cooled solution was made faintly acid with nitric acid, and the chloride estimated by the Volhard method.

The experimental results obtained for the distribution experiments at 17° are in the following table; the distribution ratio α is that of nicotine in the trichloroethylene layer to that in the water layer (both in %). Concentrations are given in g. per 100 g. of solution.

Distribution Data.

Water layer.			Trichloroethylene layer.			
Nicotine, %.	C_2HCl_3, %.	H_2O, %.	Nicotine, %.	H_2O, %.	C_2HCl_3, %.	α.
0·49	0·10	99·41	5·02	0·66	94·33	10·24
1·34	0·08	98·58	11·54	0·74	87·72	8·61
3·09	0·12	96·79	19·46	0·40	80·14	6·30
4·80	0·10	95·10	26·42	0·57	73·01	5·50
9·28	0·16	90·56	34·63	1·23	64·14	3·73
17·06	0·25	82·69	41·30	1·96	56·74	2·42
22·08	0·40	77·52	44·29	2·25	53·46	2·01
42·33	1·59	56·08	51·95	2·46	45·59	1·23
53·34	3·84	42·82	56·64	6·81	36·55	1·06

These data give the binodal curves *AB* and *CD* with the appropriate tie-lines of the figure. It was not found possible to complete the curve by means of distribution experiments, but this was effected by a " cloud-point " method. A solution of nicotine in trichloroethylene (of concentration as indicated by the general direction of the binodal curves) is made up, and the water added drop by drop from a burette. At the point just before which the mixture clouds, the composition of the resulting homogeneous solution represents concentrations that will lie on the extension of one or the other of the binodal curves. The solution, conjugate to the homogeneous solution found as above, is not made so that the method does not give tie lines. By this means two " cloud-point " solutions were found which had the compositions shown below.

Composition of " Cloud-point " Solutions.

Nicotine, %.	C_2HCl_3, %.	H_2O, %.	Nicotine, %.	C_2HCl_3, %.	H_2O, %.
60·33	18·64	21·03	60·00	23·90	16·10

When these two " cloud points " are plotted, they give the points × × in the figure, which enable the equilibrium curve to be completed. The compositions of the solutions in this table are nearly the same, and the plait-point consequently lies close to these points.

The cloud-point method also enabled equilibrium curves (without tie-lines) to be constructed. In the present instance, an arbitrary but known mixture of trichloroethylene and nicotine was first made. Water was then added from a burette, and the " cloud point " determined. A further known amount of nicotine was added to the mixture, and a new " cloud point " then ascertained. The procedure was continued until sufficient points were obtained.

We thank the Industrial Research Council, Eire, for a grant to one of us (M. O'C.).

UNIVERSITY COLLEGE, CORK. [*Received, March 11th,* 1941.]

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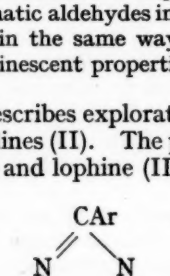
49. *Experiments in the Triazine and the Glyoxaline Series.*

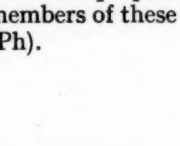
By A. H. COOK and D. G. JONES.

New derivatives of kyaphenine have been made by polymerising appropriately substituted benzonitriles in chlorosulphonic acid; a range of nitrokyaphenines was obtained by direct nitration and other means and these were converted into aminokyaphenines. Reduction of the kyaphenines in acid solution afforded triarylglyoxalines, individual members being prepared also by condensing benzil or substituted benzils with aromatic aldehydes in ammonium acetate and acetic acid. New diarylglyoxalines obtained in the same way are also described. Most of the new glyoxalines exhibit chemiluminescent properties recalling those of lophine.

THIS paper describes exploratory work on the preparation of triaryltriazines (I) and related triarylglyoxalines (II). The parent members of these series are the well-known kyaphenine (I, Ar = Ph) and lophine (II, Ar = Ph).



(I.)



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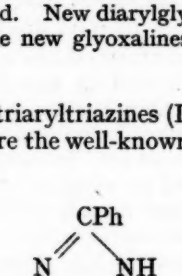

(III.)

Kyaphenine has usually been made by the polymerising action of sodium (Hofmann, *Ber.*, 1868, **1**, 198) or concentrated sulphuric acid (Pinner and Klein, *Ber.*, 1878, **11**, 764) on benzonitrile. We found the best polymerising agent to be chlorosulphonic acid (D.R.-P. 549,969), which regularly afforded yields of 40% of pure kyaphenine; thionyl chloride or sulphuryl chloride was ineffective. With sodium in benzene the only isolated product was 2 : 2 : 4 : 6-tetraphenyl-1 : 2-dihydro-1 : 3 : 5-triazine (III) (cf.

Hofmann, *loc. cit.*; Lottermoser, *J. pr. Chem.*, 1896, **54**, 132). The action of boron trifluoride alone on benzonitrile gave a sublimable product, but a little kyaphenine was formed when this was heated with ammonium fluoride.

Claus and Cloetz (*J. pr. Chem.*, 1895, **51**, 399) stated that nitration of kyaphenine afforded a tri-*m*-nitro-compound, this orientation being assigned after the isolation of *m*-nitrobenzoic acid from the products of hydrolysis. In the present experiments nitration was carried out under the most diverse conditions, but always the product, whilst agreeing approximately with the description of Claus and Cloetz, was clearly not a single trinitro-compound and indeed its nitrogen content was intermediate between that required for a dinitro- and a trinitro-compound. Although we at one time considered the formation of mixed crystals and demonstrated the feasibility of this explanation of Claus and Cloetz's results by preparing molecular compounds of nitrokyaphenines prepared in other ways, nevertheless the behaviour of the direct nitration product towards reducing agents indicated that the structure had been modified in some way other than simple nitration. It is noteworthy that another compound, more probably a true tri-*m*-nitrokyaphenine, was obtained by the hazardous method of heating *m*-nitrobenzaldehyde with nitrogen sulphide (Francis and Davis, J., 1904, **85**, 261). Seeking improved methods of preparing true nitrokyaphenines, we attempted without useful result the following methods: (*a*) Polymerisation of *o*-, *m*-, or *p*-nitrobenzonitrile or mixtures of these with benzonitrile. Sodium in benzene was without action. Sulphuric acid led either to sulphonation or to the formation of small yields of kyaphenine itself. *m*- or *p*-Nitrobenzonitrile together with benzonitrile in chlorosulphonic acid gave apparently homogeneous kyaphenine-like products, which were not identical with true mono- or di-*m*- or -*p*-nitrokyaphenine, although their composition indicated this degree of nitration. In view of the likelihood of molecular compounds being formed such experiments were abandoned. Polymerisation of nitrobenzonitriles with boron trifluoride was likewise unsuccessful. (*b*) *m*- and *p*-Nitrobenzonitriles were converted into the nitro-iminoether hydrochlorides; these could not be converted into nitrokyaphenines, although benziminoether is one source of kyaphenine (Pinner, *Ber.*, 1889, **22**, 1611). *o*-Nitrobenziminoether hydrochloride has not been described; attempts to prepare it in the way that the *m*- and the *p*-compound are obtained gave an unidentified, yellow, water-soluble compound; this was "unimolecular" but was not a hydrochloride or a hydrolysis or alcoholysis product of the nitrile. (*c*) Experiments with cyanuric chloride, aluminium chloride, and nitrobenzene, or with cyanuric chloride, sodium, and bromo- or iodo-nitrobenzene did not lead to kyaphenines (cf. Klason, *J. pr. Chem.*, 1887, **35**, 83; Krafft, *Ber.*, 1889, **22**, 1760).

A number of authentic nitrokyaphenines were at length obtained by modifying a reaction by which Eitner and Krafft (*Ber.*, 1892, **25**, 2266) synthetised kyaphenine. Ammonium chloride and aluminium chloride were heated with benzonitrile and *m*-nitrobenzoyl chloride to give m-*nitrokyaphenine*. p-*Nitrokyaphenine* was obtained similarly and by using *m*- or *p*-nitrobenzonitrile with benzoyl chloride *di*-m- and -p-*nitrokyaphenines* were prepared. The reaction failed when combinations of nitriles and acid chlorides which should have yielded *o*-nitro- or trinitro-kyaphenines were used.

The properties of the trimerides of some other nitriles were also examined. *p*-Toluonitrile was most conveniently polymerised to the kyaphenine in chlorosulphonic acid. Tri-*p*-methylkyaphenine and the calculated amount of potassium nitrate in sulphuric acid afforded a *mono*-m-*nitrotri*-p-*methylkyaphenine*, but further nitration always yielded a *trinitro*-compound. The nitro-groups entered the *m*-positions, as this trinitro-compound was also produced by the polymerisation of 2-nitro-4-cyanotoluene in chlorosulphonic acid (cf. the inertness of nitrobenzonitriles). *m*-Toluonitrile and, less readily, *o*-toluonitrile as well as *p*-chlorobenzonitrile were polymerised in chlorosulphonic acid. Only two nitro-groups could be introduced into tri-*p*-chlorokyaphenine even by prolonged nitration.

When kyaphenine is reduced by acid reagents, one nitrogen atom is eliminated from the triazine ring with formation of the glyoxaline lophine (II) (Radziszewski, *Ber.*, 1882, **15**, 1493; Scholl and Nörr, *ibid.*, 1900, **33**, 1054). The preparation of representative *amino-kyaphenines* was, however, achieved by reducing the nitrokyaphenines already prepared with phenylhydrazine, and the same reduction was also effected by sodium hyposulphite.

All the amino-compounds so obtained were sparingly soluble aromatic bases which could be diazotised in pyridine solution.

The above-mentioned conversion of the triazine into the glyoxaline ring system by acid reduction seems to be general. Tri-*p*-methylkyaphenine was converted into tri-*p*-methyllophine by zinc and acetic acid (Radziszewski, *loc. cit.*) and a well-characterised *tri*-p-*chlorolophine* was obtained similarly. Reduction of available nitrokyaphenines with zinc and acetic acid, however, afforded obvious mixtures of bases, probably isomeric aminolophines. The problem of preparing individual aminolophines was then approached by first obtaining nitrolophines of known orientation.

Lophine itself is best obtained by interaction of benzil, benzaldehyde, and ammonia or of reactants which are the equivalent of these. This method has recently been improved by working with ammonium acetate in acetic acid solution (Davidson, Weiss, and Jelling, *J. Org. Chem.*, 1937, **2**, 326). These conditions were found to be excellent for preparing a wide range of substituted glyoxalines. Benzil was, for example, replaced by *p*-nitrobenzil or phenanthraquinone with formation of glyoxalines in practically theoretical yield, though it could not be replaced by diacetyl or β-naphthaquinone. On the other hand, benzil was condensed with acetaldehyde, propaldehyde, *iso*butaldehyde, salicylaldehyde, and anisaldehyde under these conditions to give excellent yields of glyoxalines; acraldehyde, crotonaldehyde, β-methylacraldehyde, and cinnamaldehyde failed to give glyoxalines. By this reaction, combination of benzil or nitrobenzil with nitrobenzaldehydes afforded a range of *nitrolophines*. They were high-melting solids, sometimes isolated in two physical modifications; they dissolved easily in caustic alkali with production of deep red colours. They were reduced by phenylhydrazine to give good yields of *aminolophines*. Here there is no risk of ring modification and the same compounds were obtained by reduction with zinc and acetic acid. They were also high-melting diazotisable bases.

It has long been known that lophine is oxidised (*e.g.*, by sodium hypochlorite and hydrogen peroxide) with production of light. Many of the glyoxalines here described exhibited similar chemiluminescent properties, although considerable variations in colour and intensity were observed. Under the conditions recommended by Cottman, Moffet, and Moffet (*Proc. Indian Acad. Sci.*, 1938, **47**, 124) the intensity was always such that a dark room was necessary for its observation. Of those examined, the chemiluminescence of tri-*p*-chlorolophine was brightest, though it was yellower and of shorter duration than that of lophine itself. 4 : 5-*Diphenyl*-2-p-*methoxyphenyl*-, -2-methyl-, -2-*ethyl*-, and -2-iso-*propyl*-*glyoxalines* also showed luminescence, the first yellow, the others greenish-yellow. The chemiluminescence of tri-*p*-methyl-lophine was particularly persistent. *m*-Nitrolophine was the only compound of this range which exhibited luminescence and was the only nitrolophine not readily soluble in caustic alkali. Neither of the phenanthriminazoles showed any chemiluminescence.

Experimental.

Kyaphenines.—The following method (cf. F.P. 705,407) was satisfactory. Benzonitrile (25 g.) was slowly added to chlorosulphonic acid (50 c.c.) at 0° and the viscous solution was poured on ice after standing overnight; kyaphenine, so precipitated, was recrystallised from toluene, forming small white needles (17 g.), m. p. 232°. Tri-*m*- and -*p*-methylkyaphenines were obtained in the same way. *o*-Toluonitrile (5 g.) was kept with chlorosulphonic acid (10 c.c.) at 0° for 48 hours; the solid (0·5 g.) obtained by pouring the solution on ice was sublimed at 190°/0·002 mm., and the *tri*-o-*methylkyaphenine* recrystallised from acetic acid, forming stout white rods, m. p. 110° (Found: N, 12·1. $C_{24}H_{21}N_3$ requires N, 11·9%). The crude solid (4 g.) obtained from *p*-chlorobenzonitrile (5 g.) in chlorosulphonic acid (10 c.c.) as in earlier experiments was washed with alcohol and crystallised from decalin, tri-*p*-chlorokyaphenine separating in small white needles, m. p. 335° (cf. Davis, J., 1905, **87**, 1834) (Found: N, 10·4. Calc. for $C_{21}H_{12}N_3Cl_3$: N, 10·2%).

Nitrokyaphenines.—Benzonitrile (6 g.), *m*-nitrobenzoyl chloride (4 g.), ammonium chloride (5 g.), and aluminium chloride (4·5 g.) were intimately mixed and heated overnight at 140—150°. The melt was stirred with ice and concentrated hydrochloric acid, and the precipitate collected, washed with dilute acid, and crystallised from acetic acid; m-*nitrokyaphenine* separated in small white needles (2·5 g.), m. p. 206° (Found: N, 15·9. $C_{21}H_{14}O_2N_4$ requires N, 15·8%).

p-*Nitrokyaphenine* was obtained in the same way and in similar yield by using *p*- instead of *m*-nitrobenzoyl chloride; it crystallised from acetic acid in pale yellow needles, m. p. 218° (Found: N, 15·8%). *m*-Nitrobenzonitrile (6 g.), benzoyl chloride (4 g.), ammonium chloride (5 g.), and aluminium chloride (4·5 g.), treated in the same manner, yielded *di*-m-*nitrokyaphenine*, which separated from nitrobenzene as a white crystalline powder (5·5 g.), m. p. 253° (Found: N, 17·6. $C_{21}H_{13}O_4N_5$ requires N, 17·5%). *Di*-p-*nitrokyaphenine* was obtained similarly from *p*-nitrobenzonitrile; unchanged nitrile in the crude product was sublimed at 150°/0·002 mm., and the residue crystallised from nitrobenzene, forming small pale yellow plates, m. p. 297° (Found: N, 17·5). *p*-Nitrobenzonitrile and *p*-nitrobenzoyl chloride, treated in the same manner, afforded no kyaphenine but only a ketone (*dinitrocyanobenzophenone*) crystallising from acetic acid in yellow plates, m. p. 218° (Found: N, 14·6. $C_{14}H_7O_5N_3$ requires N, 14·1%). Tri-*p*-methylkyaphenine (1 g.), dissolved in concentrated sulphuric acid (5 c.c.), was treated with powdered potassium nitrate (0·9 g.). After standing overnight, the solution was poured on ice; m-*nitrotri*-p-*methylkyaphenine* was collected and recrystallised from decalin, forming a white powder (0·9 g.), m. p. 239° (Found: N, 14·9. $C_{24}H_{20}O_6N_4$ requires N, 14·5%). 2-Nitro-4-cyanotoluene (Banse, *Ber.*, 1894, **27**, 2161) was polymerised in chlorosulphonic acid in the usual manner; the product, *tri*-m-*nitrotri*-p-*methylkyaphenine*, separated from nitrobenzene as a white granular powder, m. p. 305—307° (Found: N, 17·1. $C_{24}H_{18}O_6N_6$ requires N, 17·3%). The same product was obtained by nitrating tri-*p*-methylkyaphenine with fuming nitric acid or with more than 1 equiv. of potassium nitrate in sulphuric acid. Tri-*p*-chlorokyaphenine (1·7 g.) was warmed with fuming nitric acid (5 c.c.); a vigorous reaction set in and a white solid was precipitated. The *dinitrotri*-p-*chlorokyaphenine* had m. p. 348° after crystallising from nitrobenzene (Found: N, 13·9. $C_{21}H_{10}O_4N_5Cl_3$ requires N, 13·9%).

Aminokyaphenines.—*m*-Nitrokyaphenine (1 g.) was heated with phenylhydrazine (1 c.c.) for 3 hours at 150°. The solid residue was washed with ether and dried (0·8 g.). m-*Aminokyaphenine* crystallised from decalin in small needles, m. p. 214° (Found: N, 17·3. $C_{21}H_{16}N_4$ requires N, 17·3%). Similarly *p*-nitrokyaphenine (0·5 g.) afforded p-*aminokyaphenine* (0·35 g.), which crystallised from decalin in white needles, m. p. 273° (decomp.) (Found: N, 17·4%). This compound, when warmed with acetic anhydride and a few drops of concentrated sulphuric acid gave p-*acetamidokyaphenine*, which crystallised from decalin in white needles, m. p. 315° (Found: N, 15·3. $C_{23}H_{18}ON_4$ requires N, 15·3%). Mono-*m*-nitrotri-*p*-methylkyaphenine (1 g.) similarly yielded m-*aminotri*-p-*methylkyaphenine* (0·55 g.) as a yellow powder crystallising from decalin, m. p. 231° (Found: N, 15·4. $C_{24}H_{22}N_4$ requires N, 15·3%). Tri-*m*-nitrotri-*p*-methylkyaphenine (0·7 g.) was heated with phenylhydrazine (0·5 c.c., *i.e.*, sufficient to reduce one amino-group) as in previous examples; *di*-m-*nitrotri*-m-*amino*-p-*methylkyaphenine* (0·4 g.), so obtained and crystallised from decalin, had m. p. 261° (Found: N, 18·7. $C_{24}H_{20}O_4N_6$ requires N, 18·5%). Attempts to reduce the remaining nitro-groups by this means were unsuccessful.

Lophines.—In preparing lophine itself it was found necessary to work in more dilute solution than was suggested by Radziszewski (*Ber.*, 1882, **15**, 1493). A solution of benzil (2·5 g.) and benzaldehyde (1·2 c.c.) in alcohol (75 c.c.) was saturated with gaseous ammonia for 2 hours. Lophine, m. p. 273°, separated on evaporation of the solution to 30 c.c. When benzil (15 g.), benzaldehyde (7·5 g.), and alcohol (50 c.c.) were treated with ammonia, an unidentified compound was obtained; it separated from nitrobenzene in white plates, m. p. 268°, mixed m. p. with lophine, 225—230° (Found: N, 14·2%).

Tri-*p*-chlorokyaphenine (1·5 g.) in boiling acetic acid (50 c.c.) was treated slowly with zinc dust (5 g.). After refluxing for 20 mins., the solution was filtered and evaporated in a vacuum. The residue was dissolved in alcohol, and *tri*-p-*chlorolophine* precipitated with a little water and crystallised from alcohol or decalin, forming small white needles, m. p. 268° (Found: N, 6·5. $C_{21}H_{13}N_2Cl_3$ requires N, 7·0%).

The following is typical of preparations of other glyoxalines (cf. Davidson, Weiss, and Jelling, *loc. cit.*). Benzil (3 g.), propaldehyde (0·9 g.), and ammonium acetate (15 g.) in glacial acetic acid (75 c.c.) were refluxed for 1 hour, and the solution then poured into water. The pale yellow 4 : 5-*diphenyl*-2-*ethylglyoxaline* (3·0 g.) crystallised from alcohol in pale yellow needles, m. p. 229° (Found: N, 10·9. $C_{17}H_{16}N_2$ requires N, 11·3%). The following were similarly obtained in excellent yield: 4 : 5-*diphenyl*-2-iso*propylglyoxaline* (from benzil and *iso*butaldehyde), long, pale yellow needles from alcohol, m. p. 248° (Found: N, 10·9. $C_{18}H_{18}N_2$ requires N, 10·7%); 2-o-*hydroxyphenyl*-4 : 5-*diphenylglyoxaline* (from benzil and salicylaldehyde), yellow needles from decalin, m. p. 209° (Found: N, 9·0. $C_{21}H_{16}ON_2$ requires N, 9·0%); 2-p-*methoxyphenyl*-4 : 5-*diphenylglyoxaline* (from benzil and anisaldehyde), yellow needles from alcohol or decalin, m. p. 229° (Found: N, 8·9. $C_{22}H_{18}ON_2$ requires N, 8·6%); 2-*phenyl*-4 : 5 : 9′ : 10′-

phenanthriminazole (from phenanthraquinone and benzaldehyde), white plates from aqueous pyridine (1 : 1), m. p. 314° (Found : N, 9·8. $C_{21}H_{14}N_2$ requires N, 9·5%); 2-o-*nitrophenyl*-4 : 5 : 9′ : 10′-*phenanthriminazole* (from phenanthraquinone and *o*-nitrobenzaldehyde), pale yellow needles from alcohol, m. p. 267° (Found : N, 12·4. $C_{21}H_{13}O_2N_3$ requires N, 12·1%).

Nitrolophines.—The following were obtained by the general method described above. The glyoxalines usually separated in almost quantitative yield from the boiling reaction medium : 2-o-*Nitrophenyl*-4 : 5-*diphenylglyoxaline* (from benzil and *o*-nitrobenzaldehyde), small yellow needles from alcohol, m. p. 230° (Found : N, 11·8. $C_{21}H_{15}O_2N_3$ requires N, 12·1%); 2-m-*nitrophenyl*-4 : 5-*diphenylglyoxaline* (from benzil and *m*-nitrobenzaldehyde), yellow powder from nitrobenzene or yellow needles from aqueous pyridine, m. p. 309° (Found : N, 11·6%); 2-p-*nitrophenyl*-4 : 5-*diphenylglyoxaline* (from benzil and *p*-nitrobenzaldehyde), yellow needles from aqueous alcohol, m. p. 240° (Found : N, 12·3%); 4-p-*nitrophenyl*-2 : 5-*diphenylglyoxaline* (from *p*-nitrobenzil and benzaldehyde), yellow powder from decalin, m. p. 229° (Found : N, 12·1%); 2-o-*hydroxyphenyl*-4-p-*nitrophenyl*-5-*phenylglyoxaline* (from *p*-nitrobenzil and salicylaldehyde), orange powder from decalin, m. p. 217° (Found : N, 11·6. $C_{21}H_{15}O_3N_3$ requires N, 11·7%); 2-m-*nitrophenyl*-4-p-*nitrophenyl*-5-*phenylglyoxaline* (from *p*-nitrobenzil and *m*-nitrobenzaldehyde); this crystallised from decalin sometimes in small brown plates, m. p. 226°, sometimes as a yellow powder, m. p. 256°, the conditions deciding which form should separate remaining obscure; the lower-melting form passed into the higher on heating just above its m. p. (Found : N, 14·6. $C_{21}H_{14}O_4N_4$ requires N, 14·5%).

Aminolophines.—2-*o*-Nitrophenyl-4 : 5-diphenylglyoxaline (2 g.) was heated with phenylhydrazine (2 c.c.) at 150—160° for 2 hours. The product, 2-o-*aminophenyl*-4 : 5-*diphenylglyoxaline* (1·1 g.), crystallised from aqueous alcohol in small, pale yellow needles, m. p. 196° (Found : N, 13·4. $C_{21}H_{17}N_3$ requires N, 13·4%). The following were similarly obtained : 2-m-*Aminophenyl*-4 : 5-*diphenylglyoxaline*, yellow needles, m. p. 283° (decomp.) from nitrobenzene–decalin (1 : 1) (Found : N, 13·2%); 4-p-*aminophenyl*-2 : 5-*diphenylglyoxaline*, crystallising from decalin, m. p. 245° (decomp.) (Found : N, 13·2%). The same compounds were obtained by suspending the appropriate nitro-compounds in hot acetic acid and reducing them with zinc dust. The products were isolated by evaporation of the filtered solution to dryness, solution of the residue in hot alcohol, and precipitation with water.

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IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W. 7.

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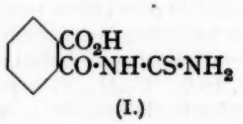
50. *Some Further Reactions of Diphenic Anhydride.*

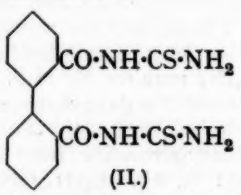
By FRANK BELL and FRED BRIGGS.

In a previous paper (J., 1938, 1561) the mode of interaction of diphenic anhydride with the simpler hydrocarbons and phenols was described; the work has been extended to include various nitrogen-containing compounds. In addition, the condensation of 4 : 4′-dinitrodiphenic anhydride with certain compounds has been examined.

PIUTTI (*Annalen*, 1882, **214**, 19) has described the interaction of phthalic anhydride with urea and thiourea to yield compounds of type (I). It is now found that the only isolable product from the interaction of diphenic anhydride with urea is diphenimide, but with thiourea *diphenoylthiourea* (II) is obtained.



(I.)



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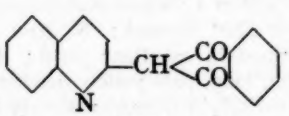


(III.)

Eibner and Hofmann (*Ber.*, 1904, **37**, 3011) established that the formula of the con-

densation product, quinophthalone, of quinaldine with phthalic anhydride is (III). It is found that diphenic anhydride readily yields an analogous *quinodiphenone*.

With aniline and methylaniline, diphenic anhydride yielded the expected N-*phenyl*- and N-*phenyl*-N-*methyl-diphenamic acids*. Conditions could not be found under which 2-*p*-aminobenzoyldiphenyl-2'-carboxylic acids could be produced by direct condensation. Dimethylaniline with diphenic anhydride gave a substance with the properties of a malachite-green.

4 : 4'-Dinitrodiphenic anhydride behaved analogously to diphenic anhydride in the following reactions. With ammonia it gave 4 : 4'-*dinitrodiphenamic acid*, with *m*-xylene or mesitylene in presence of aluminium chloride the corresponding derivatives of 4 : 4'-dinitro-2-benzoyldiphenyl-2'-carboxylic acid. Condensation with quinaldine occurred smoothly to give *quino*-4 : 4'-*dinitrodiphenone* and with thiourea there was obtained a small yield of 4 : 4'-*dinitrodiphenoylthiourea*.

When an intimate mixture of equal parts of diphenic anhydride and aluminium chloride is heated to 220° for a few minutes, the diphenic anhydride is quantitatively transformed into fluorenone-4-carboxylic acid. A similar experiment with 4 : 4'-dinitrodiphenic anhydride gave 4 : 4'-dinitrodiphenic acid as the only isolable product after decomposition of the reaction mass with hydrochloric acid. Much decomposition had occurred.

Experimental.

An asterisk indicates microanalysis by Dr. G. Weiler of Oxford.

Reactions of Diphenic Anhydride.—(a) *With aniline.* N-*Phenyldiphenamic acid* was obtained by solution of diphenic anhydride in hot aniline; stannic chloride had no influence on the course of the reaction. The acid crystallised from aqueous acetic acid in needles, m. p. 181—183° (Found: equiv., 317. $C_{20}H_{15}O_3N$ requires equiv., 317). It was recovered unchanged from boiling acetic anhydride, and underwent hydrolysis with 50% sulphuric acid to yield diphenic acid and aniline. Attempts to prepare a pure nitro-derivative were unsuccessful.

(b) *With methylaniline.* N-*Phenyl*-N-*methyldiphenamic acid* was obtained by solution of diphenic anhydride in hot methylaniline; aluminium chloride had no influence on the course of the reaction, but stannic chloride occasioned the additional formation of a dark purple colouring matter. The acid crystallised from acetic acid in needles, m. p. 181° (Found: equiv., 331. $C_{21}H_{17}O_3N$ requires equiv., 331); it was hydrolysed by 50% sulphuric acid to yield diphenic acid.

(c) *With dimethylaniline.* (i) A mixture of dimethylaniline (10 c.c.), diphenic anhydride (5 g.), and stannic chloride (5 c.c.) was heated at 110—120° for 2 hours. Excess of sodium hydroxide was then added, and unchanged dimethylaniline removed in steam. The residual solution was filtered and approximately neutralised with hydrochloric acid. The green precipitate obtained was redissolved in sodium bicarbonate solution, reprecipitated with hydrochloric acid, dried, and extracted with benzene, and the extract precipitated with light petroleum. The green product could not be crystallised from any of the common solvents. It was insoluble in 4N-sodium hydroxide but readily soluble in N/10-sodium hydroxide or sodium bicarbonate to yield a bright green solution. It dissolved in hydrochloric acid to a reddish-brown solution which dyed wool green.

(ii) A similar condensation using aluminium chloride as condensing agent resulted in a green compound similar to that previously described and also a deep blue compund. Neither of these could be obtained in a crystalline form in spite of repeated attempts. It was thought that the use of diphenic acid chloride might yield a more uniform product. Accordingly, aluminium chloride (5 g.) was added to a solution of diphenic acid chloride (5 g.) and dimethylaniline (10 c.c.) in carbon disulphide. The mixture was boiled under reflux for ½ hour, and then worked up as under (i). A small amount of a colourless material was isolated which melted at about 250° to a deep green liquid (Found *: C, 80·8; H, 6·3%). It instantly gave a deep green liquid in contact with acids and had all the properties of a dye base.

(d) *With α-picoline.* This underwent no condensation with diphenic anhydride either alone or in presence of zinc chloride.

(e) *With quinaldine.* A mixture of quinaldine (10 g.) and diphenic anhydride (10 g.) was heated at 150° for 2 hours. The product was alternately extracted with dilute hydrochloric acid and dilute aqueous ammonia until quite solid. The residual *quinodiphenone* crystallised readily from benzene or pyridine in bright yellow needles, m. p. 226—228° (Found*: C, 81·6;

H, 4·5. $C_{24}H_{15}O_2N$ requires C, 82·5; H, 4·3%), difficultly soluble in alcohol and acetone. The condensation follows essentially the same course even in the presence of zinc chloride and at higher temperature. Quinodiphenone dissolved readily in boiling alcoholic potash and on cooling a pale yellow potassium salt separated in hexagonal crystals; this regenerated the original material with hydrochloric acid.

(f) *With urea.* Diphenic anhydride (10 g.) and urea (5 g.) were maintained at 120° for 5 hours. The product yielded only diphenimide and diphenamic acid. No condensation product was isolated from the product of interaction of diphenic acid and urea in the presence of phosphorus oxychloride.

(g) *With thiourea.* As for urea. The product was separated by crystallisation from acetic acid into *diphenoylthiourea* and the more soluble diphenimide. The former formed needles containing acetic acid of crystallisation, m. p. 231° (decomp.) (Found*: C, 51·9; H, 4·4; N, 14·0; S, 14·7. $C_{16}H_{14}O_2N_4S_2,C_2H_4O_2$ requires C, 51·7; H, 4·3; N, 13·4; S, 15·3%), insoluble in sodium bicarbonate solution but easily soluble in cold sodium hydroxide solution, from which it could be precipitated unchanged. On heating to the m. p., acetic acid and hydrogen sulphide were evolved; the residue on crystallisation from acetic acid furnished diphenimide.

No condensation product was isolated from the product of interaction of diphenic acid with thiourea in the presence of phosphorus oxychloride.

(h) *With o-aminophenol, p-aminophenol and salicylic acid.* After these compounds had been heated with diphenic anhydride and stannic chloride, fluorenone-4-carboxylic acid was the only crystalline material isolated from each of the products.

2 : 7-*Dinitrophenanthraquinone.*—Crude 2-nitrophenanthraquinone (30 g., obtained as a by-product in the preparation of 4-nitrophenanthraquinone) was refluxed for ½ hour with a mixture of fuming nitric acid (400 c.c.) and sulphuric acid (50 c.c.). The resultant solution was poured into water, and the precipitate filtered off, dried, and boiled with 2 l. of acetic acid to remove the more soluble 2 : 5-dinitrophenanthraquinone. The residual 2 : 7-dinitrophenanthraquinone crystallised readily from boiling nitrobenzene. Yield, 26·5 g.; m. p. 298°. On oxidation with potassium dichromate, 78·5 g. of this quinone gave 83·5 g. of purified 4 : 4′-dinitrodiphenic acid. The acid was readily converted into the anhydride by the method previously described (J., 1927, 1697).

Reactions of 4 : 4′-*Dinitrodiphenic Anhydride.*—(a) *With ammonia.* Powdered 4 : 4′-dinitrodiphenic anhydride rapidly dissolved in warm 15% ammonia solution to give 4 : 4′-*dinitrodiphenamic acid*, which, after recrystallisation from acetic acid, formed prisms, m. p. 237—239° (decomp.) (Found: equiv., 328. $C_{14}H_9O_7N_3$ requires equiv., 331).

(b) *With* m-*xylene.*—Powdered aluminium chloride (6 g.) was added to a suspension of 4 : 4′-dinitrodiphenic anhydride (6 g.) in *m*-xylene. After standing overnight, the mixture was decomposed with hydrochloric acid, the excess of xylene removed in steam, and the residue dissolved in sodium hydroxide solution, reprecipitated with hydrochloric acid, and purified by crystallisation from acetic acid. 4 : 4′-*Dinitro*-2-2″ : 4″-*dimethylbenzoyldiphenyl*-2′-*carboxylic acid* formed small prisms, m. p. 207° (Found*: C, 62·9; H, 3·9. $C_{22}H_{16}O_7N_2$ requires C, 62·9; H, 3·8%); warmed at 120° for ¼ hour with sulphuric acid, it yielded a sparingly soluble sulphonic acid.

(c) *With mesitylene.* As for *m*-xylene. 4 : 4′-*Dinitro*-2-2″ : 4″ : 6″-*trimethylbenzoyldiphenyl*-2′-*carboxylic acid* was separated from resinous acidic material by preparing its sparingly soluble sodium salt. The acid crystallised from acetic acid in needles, m. p. 183—185° (Found: equiv., 438. $C_{23}H_{18}O_7N_2$ requires equiv., 434). On heating with sulphuric acid at 100° for ¼ hour it gave 4 : 4′-dinitrodiphenic acid.

(d) *With quinaldine. Quino*-4 : 4′-*dinitrodiphenone*, obtained by heating 4 : 4′-dinitrodiphenic anhydride with quinaldine at 170—190° for 2 hours, crystallised from nitrobenzene in orange needles, m. p. above 300° (Found*: C, 65·6; H, 3·3. $C_{24}H_{12}O_6N_2$ requires C, 65·6; H, 3·3%).

(e) *With thiourea.* 4 : 4′-*Dinitrodiphenoylthiourea*, obtained by heating the anhydride with thiourea at 130—140° for 2 hours, crystallised from nitrobenzene in small, pale yellow needles, m. p. 239° (decomp.) (Found*: C, 43·7; H, 2·6; S, 13·7. $C_{16}H_{12}O_6N_6S_2$ requires C, 42·9; H, 2·6; S, 14·3%).

(f) *With ethylbenzene, phenol, or resorcinol.* No crystallisable material could be isolated from the products of interaction of the anhydride with phenol or resorcinol (both in presence of stannic chloride) or ethylbenzene (in presence of aluminium chloride).

MUNICIPAL TECHNICAL COLLEGE, BLACKBURN. [*Received, March 19th*, 1941.]

51. 5-*Amino*-1-*aryl*-3-*methylpyrazoles*.

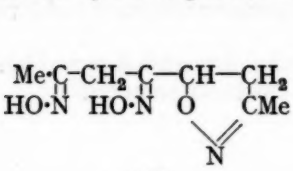
By Frank Bell.

5-Amino-1-phenyl-3-methylpyrazole has been prepared by several distinct methods, but it is not possible from the literature to evaluate the relative efficiencies of these methods or ascertain their suitability for the preparation of analogous compounds. The methods have therefore been resurveyed.

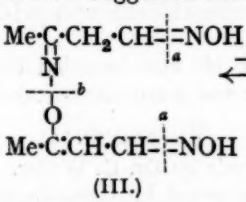
According to Claisen (*Ber.*, 1909, **42**, 67), 5-amino-1-phenyl-3-methylpyrazole is obtained by lengthy boiling of 5-methyl*iso*oxazole with phenylhydrazine. This *iso*oxazole is obtained by heating with N/2-hydrochloric acid the compound $C_8H_{13}O_3N_3$, which is prepared by interaction of sodioacetoacetaldehyde with hydroxylamine hydrochloride (Claisen, *Ber.*, 1891, **24**, 139). It is now found that about 40 g. of sodioacetoacetaldehyde are required to prepare 5 c.c. of 5-methyl*iso*oxazole. This does not accord with Claisen's simple representation (I) of the decomposition of the intermediate " oxymethylene acetonesesquioxime." The formula (II) put forward for this sesquioxime by Scholl (*Ber.*, 1897,

$$C_8H_{13}O_3N_3 + HCl = 2C_4H_5ON + NH_2{\cdot}OH,HCl \quad (I.)$$

30, 1292) was rejected by Claisen (*loc. cit.*, p. 64, footnote) on the ground that it cannot be reconciled with the smooth decomposition of the compound by hydrochloric acid. With very dilute acid the product is 5-methyl*iso*oxazole, but with more concentrated acid 3-methyl*iso*oxazole is obtained; 5-methyl*iso*oxazole is not converted into 3-methyl*iso*oxazole by heating with acids. It is now suggested that the sesquioxime is satisfactorily



(II.)



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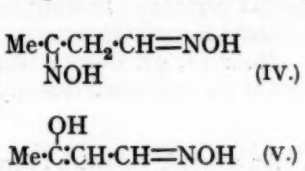
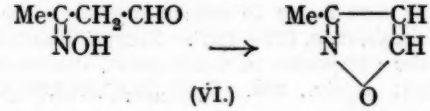


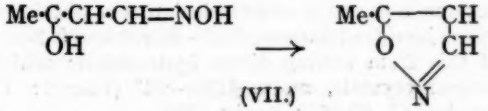
(IV.)

(V.)

represented by (III), produced by interaction of one molecule of acetoacetaldehydedioxime (IV) with one molecule of acetoacetaldehydemonoxime (V). Hydrolysis of (III) with hydrochloric acid could follow one of two courses: either (i) linkage (*a*) is severed first; when, subsequently, linkage (*b*) is severed, the only *iso*oxazole which can be produced is 3-methyl*iso*oxazole (VI); or (ii) linkage (*b*) is severed first, in which case 5-methyl*iso*-



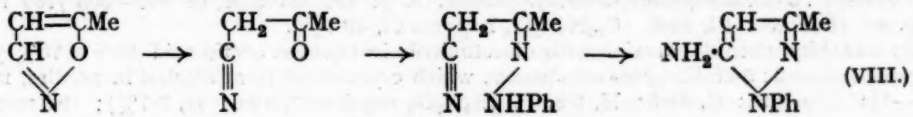
(VI.)



(VII.)

oxazole (VII) can be produced from either of the primary decomposition products. The experimental results would indicate that the mode of decomposition is conditioned by the strength of the acid.

The conversion of 5-methyl*iso*oxazole into 5-amino-1-phenyl-3-methylpyrazole by the action of boiling phenylhydrazine is mentioned by Claisen, who added that he would give details in a future communication. It is now found that the conversion goes very unsatisfactorily. Only 0·5 g. of the amine was obtained from 5 c.c. of the *iso*oxazole after this had been boiled with phenylhydrazine for six hours. The probable mechanism of the



(VIII.)

change (VIII) appears to be that the methyl*iso*oxazole first yields cyanoacetone, which reacts to give cyanoacetonephenylhydrazone, and this undergoes isomerisation to the

aminopyrazole. If this is so, the yield should be improved by dissolving the methyl*iso*oxazole in warm potassium hydroxide solution to produce cyanoacetone, preparing from this the phenylhydrazone, and then isomerising the latter by hydrochloric acid. Actually 1·5 g. of purified aminopyrazole were obtained from 5 c.c. of methyl*iso*oxazole by this method.

Cyanoacetonephenylhydrazone is much more easily prepared from diacetonitrile. Moir (J., 1902, **81**, 101) has described the preparation of diacetonitrile. He states that the " yield leaves much to be desired," but does not record the exact percentage. In the present experiments yields were obtained varying between 44 and 49%. Mohr's method (*J. pr. Chem.*, 1909, **79**, 14) of converting this into the phenylhydrazone of cyanoacetone gave yields of 89—92%, and the subsequent conversion of this into 5-amino-1-phenyl-3-methylpyrazole by warm 6N-hydrochloric acid gave a yield of 80%. This satisfactory method of preparing aminopyrazoles was used to obtain 5-*amino*-1-(2′-*chlorophenyl*)- and -1-(2′ : 5′-*dichlorophenyl*)-3-*methylpyrazoles*.

Michaelis and Brust (*Annalen*, 1905, **339**, 134) have described the preparation of 5-amino-1-phenyl-3-methylpyrazole by heating 5-chloro-1-phenyl-3-methylpyrazole methochloride (antipyrine chloride) with ammonium carbonate under pressure. They state that the more accessible 5-chloro-1-phenyl-3-methylpyrazole undergoes no reaction with either ammonium carbonate or ammonia–zinc chloride. It is now found that the latter can be recovered unchanged after heating with powdered sodamide for some hours. In contrast with the description given by Michaelis, it was found that, when antipyrine is boiled with phosphorus oxychloride for twelve hours, it is entirely converted into 5-chloro-1-phenyl-3-methylpyrazole-4-phosphinic acid (Michaelis and Pasternack, *Ber.*, 1899, **32**, 2411); with shorter periods of heating, antipyrine chloride was produced together with much 5-chloro-1-phenyl-3-methylpyrazole.

Mohr (*J. pr. Chem.*, 1909, **79**, 16) has recorded that 1-phenyl-3-methyl-5-pyrazolone cannot be converted directly into the 5-aminopyrazole by the Bucherer reaction.

Experimental.

An asterisk indicates microanalysis by Dr. G. Weiler.

o-Chlorophenylhydrazine was prepared by Hewitt's method (J., 1891, **59**, 209; 1893, **63**, 868). Diacetonitrile (16 g.) was added to a solution of *o*-chlorophenylhydrazine (34 g.) in acetic acid (40 c.c.) and water (40 c.c.). The mixture was warmed on a steam-bath for ½ hour, diluted with water, and kept until the oil which separated had solidified. This *cyanoacetone-o-chlorophenylhydrazone* had m. p. 74—77° after two recrystallisations from alcohol (Found* : C, 58·4; H, 4·9. $C_{10}H_{10}N_3Cl$ requires C, 57·8; H, 4·8%). 20 G. of this compound were added to a mixture of concentrated hydrochloric acid (40 c.c.) and water (20 c.c.). The mixture became hot and a clear solution was obtained, which soon began to deposit crystals of the *hydrochloride* of 5-*amino*-1-(2′-*chlorophenyl*)-3-*methylpyrazole*, m. p. 122—125°. Recrystallisation of this from boiling dilute hydrochloric acid gave the compound in transparent, diamond-shaped crystals, m. p. 123—126° (Found : Cl*, 24·3; equiv., 284. $C_{10}H_{10}N_3Cl,HCl,2H_2O$ requires Cl, 25·3%; equiv., 280).

2 : 5-Dichlorophenylhydrazine was prepared by the method of Noelting and Kopp (*Ber.*, 1905, **38**, 3510). 12 G. were mixed with ethyl acetoacetate and warmed on the steam-bath for several hours. The product, which was solid at room temperature, on recrystallisation from alcohol gave *ethyl acetoacetate* 2 : 5-*dichlorophenylhydrazone* in plates (13·3 g.), m. p. 66—68° (Found* : C, 50·6; H, 4·9. $C_{12}H_{14}O_2N_2Cl_2$ requires C, 49·8; H, 4·8%). When this compound was heated with phosphorus oxychloride, the mixture soon changed to a brown plastic mass. After cooling, ice was added, and the product extracted with ether. The extract was dried with potassium carbonate and distilled under diminished pressure, yielding 5-*chloro*-1-(2′ : 5′-*dichlorophenyl*)-3-*methylpyrazole*, b. p. 195°/25 mm. or 303—305°/760 mm., m. p. 44° (Found* : Cl, 40·8. $C_{10}H_7N_2Cl_3$ requires Cl, 40·7%).

2 : 5-Dichlorophenylhydrazine with diacetonitrile in aqueous acetic acid gave a 70% yield of *cyanoacetone*-2 : 5-*dichlorophenylhydrazone*, which crystallised from alcohol in needles, m. p. 112—114° (Found* : C, 50·3; H, 3·8. $C_{10}H_9N_3Cl_2$ requires C, 49·6; H, 3·7%); the mother-liquor furnished acetyl-2 : 5-dichlorophenylhydrazine, m. p. 160°. Cyanoacetonedichlorophenylhydrazone (13 g.) with hydrochloric acid (52 c.c.) soon yielded a warm clear solution; this subsequently deposited prisms, m. p. 214—220°, of the *hydrochloride* of 5-*amino*-1-(2′ : 5′-

dichlorophenyl)-3-*methylpyrazole*, which could be readily recrystallised from boiling dilute hydrochloric acid (Found: Cl*, 37·9; equiv., 283. $C_{10}H_9N_2Cl_2$,HCl requires Cl, 38·2%; equiv., 279).

The author thanks Imperial Chemical Industries Ltd. (Dyestuffs Group) for a gift of chemicals.

MUNICIPAL TECHNICAL COLLEGE, BLACKBURN. [*Received, March 19th*, 1941.]

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52. *A Synthesis of Dihydroindole, Dihydrothionaphthen, and Dihydrobenzofuran.*

By G. M. BENNETT and MOSTAFA MAHMOUD HAFEZ.

Simple methods are described by which the three heterocyclic substances named in the title may be obtained in good yield from β-phenylethyl alcohol through its *o*-amino-derivative.

SYNTHESES have been described of 2 : 3-dihydroindole (indoline), 2 : 3-dihydrothionaphthen, and 2 : 3-dihydrobenzofuran (coumaran) by various methods, yet no simple set of analogous syntheses of the three substances appears to have been recorded. Thus v. Braun and his collaborators (*Ber.*, 1925, **58**, 2165) obtained dihydrothionaphthen from *o*-amino-β-chloroethylbenzene and Ferber (*Ber.*, 1929, **62**, 183) converted the same substance into dihydroindole, but the synthesis of dihydrobenzofuran has proceeded from *o*-bromophenyl β-bromoethyl ether (Stoermer and Göhl, *Ber.*, 1903, **36**, 2873) or β-phenoxyethyl alcohol (Rindfusz, *J. Amer. Chem. Soc.*, 1919, **41**, 665; 1920, **42**, 157).

In the course of other work we have found that *o*-amino-β-phenylethyl alcohol can be readily converted into each of these three heterocyclic substances in good yield. Indoline is obtained by heating this base with hydrochloric acid and making alkaline, or directly by the action of benzenesulphonyl chloride on the amine in cold aqueous alkali; a solution of the base, diazotised and neutralised with sodium hydrogen carbonate, yields dihydrobenzofuran; and, finally, if a sulphur atom is introduced by the Leuckhardt process, the product is at once converted into dihydrothionaphthen when warmed with acid.

The great ease of the ring closure in these instances is not only the result of the obvious steric factor: there is also a specially enhanced reactivity of the hydroxyl group, a study of which will be described in another paper.

The ready formation of the indole ring from *o*-amino-β-phenylethyl alcohol and analogous compounds may, as Dr. H. A. Krebs has pointed out to us, indicate the way in which indole is formed from tryptophan by bacterial action, and one of us is studying the matter from this point of view.

EXPERIMENTAL.

Preparation of o-*Amino*-β-*phenylethyl Alcohol.*—The crude mixture of isomeric nitro-β-phenylethyl alcohols obtained by the method of Sabetay (*Bull. Soc. chim.*, 1931, **49**, 3; compare Ferber, *loc. cit.*) was freed from solvent, inoculated with the *p*-nitro-alcohol, and kept in the cold. The material which crystallised was filtered off and twice recrystallised from alcohol; it had m. p. 65° (Ferber gives 60—61°). The filtrate was a deep red oil, to which was added any further similar material recovered from the mother-liquors of the recrystallisation of the *p*-isomeride. This oil was separated into two fractions by distillation at low pressure with a spiral glass fractionating column: (I) b. p. 136°/2 mm. and (II) b. p. 136—145°/2 mm. The first distillate (III) obtained on redistillation of (I) was the pure *o*-nitro-β-phenylethyl alcohol, since the refractive index remained constant [$n_D^{25°}$ of crude mixture 1·5682; of (I) 1·5623; of (III) 1·5602, constant to ± 0·0002. Sabetay gives $n_D^{22°}$ 1·5620]. Further quantities of the *o*-isomeride were obtained by freezing out and redistilling the later fractions.

Reduction of the *o*-nitro-alcohol by Sabetay's method was improved by extracting the product from the concentrated solution with ether and then distilling it. The *o*-amino-alcohol is a colourless, viscous oil of b. p. 166—167°/12 mm. or 155° 5 mm. The *N*-acetyl derivative

crystallises from benzene in small prisms with a high double refraction, m. p. 101·5° (Found: C, 66·8; H, 7·2; N, 8·0. Calc.: C, 66·9; H, 7·3; N, 7·8%).

o-*Benzamido*-β-*phenylethyl alcohol* crystallises from alcohol in nearly rectangular plates with an oblique extinction, m. p. 168° (Found: C, 74·4; H, 5·9; N, 6·0. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·2; N, 5·8%).

Synthesis of Indoline.—(a) *o*-Amino-β-phenylethyl alcohol, heated for 4 hours with concentrated hydrochloric acid (5 parts) at 130—140°, gave the hydrochloride of *o*-amino-β-phenylethyl chloride in almost quantitative yield, which crystallised in fine needles, m. p. 174°, from alcohol–ether (Found: C, 50·0; H, 5·7. Calc.: C, 50·0; H, 5·7%). v. Braun and Sobecki (*Ber.*, 1911, **44**, 2158) prepared this substance by the hydrolysis of its *N*-benzoyl derivative (from benzoylindoline by ring fission) but they gave its m. p. as 205°. This is the correct figure for the m. p. of the *p*-isomeride (v. Braun and Gawilow, *Ber.*, 1912, **45**, 1274) and was perhaps due to an error in transcription.

The hydrochloride was made alkaline with sodium hydroxide, the cyclic base distilled in steam and extracted from the distillate with ether, and the solution dried over sodium sulphate or sodium hydroxide and distilled. Indoline was thus obtained as a colourless oil, b. p. 230°, yielding a benzenesulphonyl derivative, m. p. 133° (Ferber gives 132°, *loc. cit.*). The p-*toluenesulphonyl* derivative crystallises from 75% alcohol in prisms with a high double refraction and a straight extinction, m. p. 99° (Found: C, 66·3; H, 5·5; N, 5·5; S, 11·9. $C_{15}H_{15}O_2NS$ requires C, 65·9; H, 5·5; N, 5·1; S, 11·7%). The *acetyl* derivative separates from alcohol in minute white needles with an oblique extinction, m. p. 105° (Found: C, 74·3; H, 6·8; N, 8·8. $C_{10}H_{11}ON$ requires C, 74·5; H, 6·8; N, 8·7%).

(b) *o*-Amino-β-phenylethyl alcohol (3·3 g.), dissolved in aqueous sodium hydroxide (50 c.c., 10%), was shaken for ½ hour with benzenesulphonyl chloride (3·3 c.c.). A trace of solid which separated was benzenesulphonylindoline. The free base in solution was removed in steam and collected from the distillate in ether, and the extract dried and distilled. Indoline was thus obtained in good yield, b. p. 230°, giving the benzenesulphonyl derivative, m. p. 133°.

Synthesis of 2 : 3-*Dihydrothionaphthen.*—*o*-Amino-β-phenylethyl alcohol (24 g.), dissolved in hydrochloric acid (45 c.c. of concentrated acid, 135 c.c. of water), was diazotised at 5° and slowly added to a stirred solution of potassium xanthate (45 g. in 80 c.c. of water) at 65—70°. After the mixture had been heated until evolution of gas had ceased, and cooled, the xanthic ester was removed in ether, and the solution evaporated. This ester was hydrolysed by cautiously adding potassium hydroxide (25 g. in 10 c.c. of water with 40 c.c. of alcohol); when the mixture had cooled, the alcohol was quickly distilled away in a current of nitrogen. The solution was then diluted, extracted once with ether to remove any material insoluble in alkali, acidified with dilute sulphuric acid, and heated on the water-bath for ½ hour. The crude dihydrothionaphthen separated as an oil and was removed in ether and distilled at 105—107°/13·5 mm. (Found: C, 69·1; H, 6·4; S, 23·9. Calc.: C, 70·6; H, 5·9; S, 23·5%). The yield of material, b. p. 233—234°, was almost quantitative. The mercurichloride had m. p. 127—128° (v. Braun gives 128—129°). Heating with an excess of hydrogen peroxide gave the sulphone, m. p. 98° (Found: C, 57·0; H, 4·7. Calc.: C, 57·1; H, 4·7%). When the oil was heated for 2 hours at 200—205° with half its weight of sulphur, and the mixture distilled in steam, thionaphthen was obtained as an oil, oxidised by hydrogen peroxide to the sulphone, m. p. 137—138° (Found: S, 19·1. Calc.: S, 19·3%).

Synthesis of 2 : 3-*Dihydrobenzofuran.*—*o*-Amino-β-phenylethyl alcohol (21 g.) was diazotised in sulphuric acid solution (15 c.c. of concentrated acid in 60 c.c. of water; 11 g. of sodium nitrite) and, when the reaction was complete, sodium hydrogen carbonate added in excess. The mixture was warmed until evolution of nitrogen had ceased; it was then made alkaline with sodium hydroxide, the product taken over in steam, and the distillate extracted with ether. The extract was washed with alkali and with water, dried, and distilled, dihydrobenzofuran being obtained, b. p. 84°/17 mm. or 188°/1 atm. (yield, 50%) (Found: C, 80·1; H, 6·5. Calc.: C, 80·0; H, 6·7%). The substance gave the characteristic violet coloration with ferric chloride and sulphuric acid. With cold saturated alcoholic picric acid it yielded a picrate, m. p. 76°, which lost dihydrobenzofuran on standing in the desiccator.

We make grateful acknowledgment of the assistance one of us has received from the Egyptian Government.

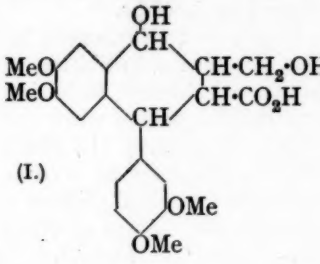
UNIVERSITY OF LONDON, KING'S COLLEGE. [*Received, March 27th*, 1941.]

53. *The Constituents of Natural Phenolic Resins. Part XIX. The Action of Formalin on 4-Keto-6 : 7-dimethoxy-1-veratryl-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylic Acid.*

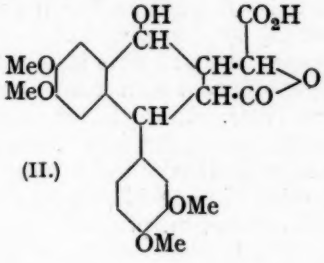
By Robert D. Haworth and George Sheldrick.

Formalin reacts almost quantitatively with cold alkaline solutions of 4-keto-6 : 7-dimethoxy-1-veratryl-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylic acid, yielding a substance with ketonic, alcoholic, and lactonic properties. The reactions of the product indicate that it has structure (V).

In the work described in Part II (J., 1935, 636) the compounds (I) and (II) were synthesised and converted by the action of heat into the α- and the β-form respectively of the lactone (III; R = H). Attempts to isolate the expected lactone (III; R = OH) or the dihydronaphthalene dehydration product were unsuccessful, and, as lactones of type (III; R = OH) are of interest in connection with the chemistry of picropodophyllin (see J., 1935, 1576; 1938, 348), an alternative route involving the action of formalin on 4-keto-6 : 7-dimethoxy-1-veratryl-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylic acid (IV) was examined. Most of the experimental work described in this communication was carried out in 1935 and a structural interpretation of the reaction, based on some new analytical results and also on the additional knowledge emerging in the meantime from other investigations in this series, is now possible.



(I.)



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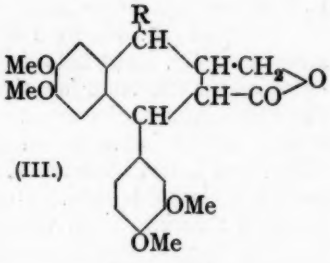

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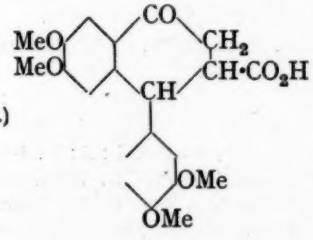
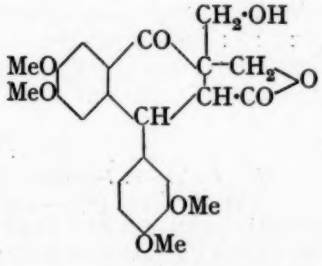
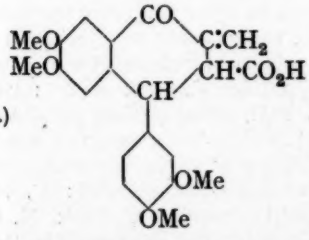


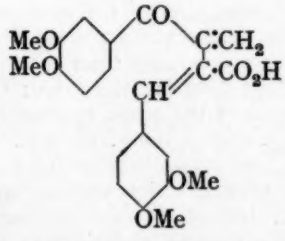
(IV.)



(V.)



(VI.)



(VII.)

An alkaline solution of the acid (IV) reacts at room temperature with excess of formalin, yielding a *substance* (A) which separates from methyl alcohol in a form, m. p. 174°, from acetone in a form, m. p. 120°, and from benzene in a form, m. p. 103—104°, containing two molecules of solvent of crystallisation. Further work is required to determine the relationship between the two unsolvated forms, m. p. 174° and 120°, but they

are closely related and the reactions and derivatives described below are given by either modification. The analytical data of the unsolvated forms agree with the formula $C_{23}H_{24}O_8$, and suggest the elimination of water from a primary condensation product of two molecules of formaldehyde with one molecule of acid (IV). Zerewitinoff determinations and the formation of a crystalline *monoacetyl* derivative, m. p. 160—162°, show the presence of one hydroxyl group in the substance (A), which also possesses feeble ketonic properties, prolonged treatment yielding a *semicarbazone*, m. p. 242—244° (decomp.). The insolubility in sodium carbonate solution and the recovery after attempted esterification with methyl-alcoholic hydrogen chloride show that (A) is not a carboxylic acid. It dissolved very slowly in cold dilute sodium hydroxide solution, but more rapidly on warming with the evolution of formaldehyde, which was isolated as the dimedon derivative, m. p. 183°. Acidification of the alkaline residue liberated a *carboxylic acid* (B), m. p. 175—177°, which slowly crystallised from benzene–light petroleum and has the composition $C_{22}H_{22}O_7$.

The properties of (A) are consistent with structure (V), and the ready elimination of formaldehyde is analogous to the reversed aldol reactions discussed by Kenner and collaborators (J., 1928, 2698; 1930, 919. See also Welch, J., 1930, 257). The presence of at least one hydroxymethyl group, at position 3, was established by the reduction of (V) with amalgamated zinc and hydrochloric acid; an oily product was obtained which yielded 6 : 7-dimethoxy-1-veratryl-3-methylnaphthalene (J., 1938, 810) on heating with selenium. The absence of the readily detectable dehydroguaiaretic acid dimethyl ether (6 : 7-dimethoxy-1-veratryl-2 : 3-dimethylnaphthalene) in the dehydrogenation products is consistent with structure (V) and excludes an alternative structure in which the second hydroxymethyl group is associated with position 2 of the naphthalene nucleus.

The acid (B), obtained from (A) by elimination of formaldehyde and represented by structure (VI), lacks ketonic properties and resists lactonisation. A similar inhibition of ketonic and ethylenic functions is observed with many αβ-unsaturated ketones, including the open-chain analogues of type (VII). In the latter case lactonisation occurs when the ketonic group is destroyed during conversion into a naphthalene derivative (J., 1935, 1576), and it has been found that reduction of the ketonic group in (VI) may be accompanied by lactonisation. Reduction of the acid (VI) by Clemmensen's method yielded a complex mixture, from which a lactone, m. p. 209°, identical with the β-form of (III; R = H) was isolated in small yield, together with an acid, m. p. 220—222°, which has been identified by comparison with an authentic specimen of 6 : 7-dimethoxy-1-veratryl-3-methyl-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylic acid (J., 1938, 812).

The direct conversion of (IV) and (VI), or its hydration product, has not been realised in spite of numerous variations of the experimental conditions.

Experimental.

Lactone of 4-Keto-6 : 7-dimethoxy-1-veratryl-3 : 3-bishydroxymethyl-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylic Acid (V).—A solution of the acid (IV) (10 g.) (J., 1935, 641) in 8% sodium hydroxide solution (20 c.c.) and 40% formalin (20 c.c.) was kept for 12 hours at room temperature. After dilution with water (40 c.c.) the solution was acidified with concentrated hydrochloric acid, and the turbid solution extracted twice with ether and twice with chloroform. The combined extracts were dried with sodium sulphate, the solvents removed, and the semi-solid residue crystallised from methyl alcohol, giving colourless prisms (9·8 g.), m. p. 174° (Found : C, 64·2, 64·4; H, 5·8, 6·0; OH, 4·4. $C_{23}H_{24}O_8$ requires C, 64·5; H, 5·7; OH, 4·0%). Crystallisation of the crude product or the form, m. p. 174°, from acetone yielded colourless prisms, m. p. 120° (Found : C, 64·3; H, 5·9; OH, 4·3%), which were converted into the form, m. p. 174°, on crystallisation from methyl alcohol. Either of these forms separated from benzene in prisms, which softened at 75° and melted at 103—104° (Found : C, 71·8, 71·8; H, 6·3, 6·2; loss at 80° in a vacuum, 26·2. $C_{23}H_{24}O_8,2C_6H_6$ requires C, 71·9; H, 6·2; loss, 26·7%). The *monoacetyl* derivative, prepared in 95% yields by boiling any of the three forms of (V) with acetic anhydride for 2 hours, crystallised from methyl alcohol in colourless prisms, m. p. 160—162° [Found : C, 63·6, 63·9; H, 5·6, 5·9; acetyl (Freudenberg), 8·5, 8·9. $C_{25}H_{26}O_9$ requires C, 63·8; H, 5·6; acetyl, 9·1%], which yielded the lactone (V) on hydrolysis with toluene-*p*-sulphonic acid during the acetyl estimation. The *semicarbazone*, obtained by refluxing with semicarbazide hydrochloride and potassium acetate in alcohol for 48 hours, separated

from methyl alcohol in micro-crystals, m. p. 242—244° (decomp.) (Found : N, 9·0. $C_{21}H_{17}O_6N_3$ requires N, 8·7%).

4-Keto-6 : 7-dimethoxy-1-veratryl-2-methylene-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylic Acid (VI).—After the lactone (V) (2 g.) and 5% sodium hydroxide solution (50 c.c.) had been warmed on the water-bath for 1 hour, the mixture was concentrated to about half bulk, and the distillate warmed for 15 minutes with an alcoholic solution of dimedon. The formaldehyde dimedon compound, m. p. 183°, was collected after standing overnight. The alkaline residue was acidified with concentrated hydrochloric acid, and the gummy product extracted three times with ether. The acid was removed from the extract by washing with sodium bicarbonate solution, recovered, taken up in ether, and dried with sodium sulphate. Removal of the ether left an oil, which crystallised very slowly from benzene–light petroleum (b. p. 60—80°). A second crystallisation (carbon) yielded colourless prisms (0·6 g.), m. p. 175—177° (Found : C, 66·5, 66·4; H, 5·3, 5·3. $C_{22}H_{22}O_7$ requires C, 66·3; H, 5·5%).

Conversion of (V) *into* 6 : 7-*Dimethoxy-1-veratryl-3-methylnaphthalene.*—The lactone (V) (2 g.), amalgamated zinc (10 g.), and concentrated hydrochloric acid (10 c.c.) were refluxed for 24 hours. After dilution with water the mixture was extracted with ether, washed several times with 1% sodium hydroxide solution, dried, and distilled. The fraction (1 g.), b. p. 240—270°/0·4 mm., was heated with selenium (1 g.) at 280—300° for 24 hours. The product was isolated with chloroform, the solvent removed, and the residue taken up in ether, filtered from impurities, and purified by sublimation at 0·2 mm. and finally by crystallisation from light petroleum (b. p. 60—80°). 6 : 7-Dimethoxy-1-veratryl-3-methylnaphthalene was obtained in stout prisms (0·1 g.), m. p. 140—141°, identical with the specimen obtained previously (J., 1937, 1646; 1938, 812). The picrate, red needles, m. p. 133°, was also prepared.

Conversion of (VI) *into* (II; R = H) *and* 6 : 7-*Dimethoxy-1-veratryl-3-methyl-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylic Acid.*—The acid (VI) (4 g.), amalgamated zinc (20 g.), and concentrated hydrochloric acid (20 c.c.) were refluxed for 36 hours. The product, isolated with chloroform, was a brown oil, which was dissolved in warm 8% sodium hydroxide solution (20 c.c.). The neutral impurities, removed in ether, were not investigated. The alkaline layer was acidified with concentrated hydrochloric acid and heated on the water-bath for 1 hour, and the product extracted with chloroform. After removal of carboxylic acids and phenols by shaking with dilute sodium hydroxide solution, the lactonic product was recovered from the chloroform and purified by sublimation at 0·4 mm. The sublimate crystallised from methyl alcohol–chloroform in stout prisms (0·02 g.), m. p. 209—210°, which did not depress the m. p. of a specimen of the β-form of (III; R = H) (J., 1935, 643). The sodium hydroxide solution containing carboxylic acids and phenolic impurities was acidified, and the product (1·5 g.), isolated with chloroform, was refluxed with methyl-alcoholic hydrogen chloride (30 c.c.) for 12 hours, diluted with water, and extracted with ether. The extract was washed several times with 2% sodium hydroxide solution, which removed a considerable quantity of dark-coloured impurity, and evaporated. The residual oil was hydrolysed with 10% methyl-alcoholic potassium hydroxide (10 c.c.), most of the alcohol was removed, and after the addition of water the mixture was acidified and extracted with ether. The extract yielded a crude brown acid, which was taken up in sodium bicarbonate solution, filtered from impurities, recovered from the filtrate, dried, and crystallised three times from benzene (carbon); 6 : 7-dimethoxy-1-veratryl-3-methyl-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylic acid was obtained in colourless nodules (0·2 g.), m. p. 220—222°, which gave no depression in m. p. when mixed with the specimen synthesised previously (J., 1938, 813).

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UNIVERSITY OF SHEFFIELD.
[*Received, April 1st,* 1941.]

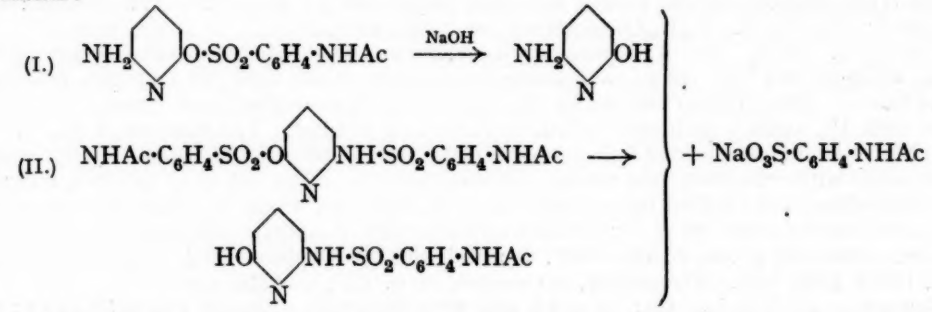
54. *The Condensation of 6-Amino-2-hydroxypyridine with p-Acetamidobenzenesulphonyl Chloride.*

By MONTAGUE A. PHILLIPS.

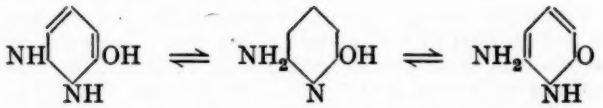
When 6-amino-2-hydroxypyridine sulphate in suspension in pyridine is condensed with *p*-acetamidobenzenesulphonyl chloride, *6-amino-2-pyridyl* p-*acetamidobenzenesulphonate* and not 6-hydroxy-2-(*p*-acetamidobenzenesulphonamido)pyridine, is formed. The amino-compound corresponding to the latter compound is obtained by alkaline hydrolysis of 6-p-*acetamidobenzenesulphonamido-2-pyridyl* p-*acetamido-*

benzenesulphonate, which is itself formed from the above aminopyridyl ester by further condensation with the sulphonyl chloride.

WHEN 6-amino-2-hydroxypyridine sulphate in suspension in pyridine is treated with one equivalent of *p*-acetamidobenzenesulphonyl chloride, condensation proceeds mainly on the hydroxy- and not on the amino-group, 6-*amino-2-pyridyl* p-*acetamidobenzenesulphonate* (I) being obtained in good yield together with a small amount of 6-p-*acetamidobenzenesulphonamido-2-pyridyl* p-*acetamidobenzenesulphonate* (II). This compound is more readily obtained from the ester (I) by further condensation in pyridine with one equivalent of the acid chloride. These esters are readily hydrolysed by warm dilute sodium hydroxide solution :



That condensation proceeds in the first instance on the hydroxy-group may be related to the peculiar tautomeric structure of the aminohydroxypyridine, which, like all other 2-amino-pyridines and -quinolines examined in this laboratory, does not give dyes when treated with nitrous acid and subsequently with the usual coupling reagents and hence presumably does not contain a true amino-group.



The amino-ester (I), when treated with anhydrous hydrogen chloride in alcohol, gives 6-*amino-2-pyridyl* p-*aminobenzenesulphonate*. 6-*Hydroxy*-2-(p-*aminobenzenesulphonamido*)-*pyridine*, like the parent 2-(*p*-aminobenzenesulphonamido)pyridine (Phillips, this vol., p. 9), is exceedingly stable to boiling sodium hydroxide solution and readily hydrolysed by hot mineral acids.

EXPERIMENTAL.

6-*Amino-2-pyridyl* p-*Acetamidobenzenesulphonate* (I).—To a suspension of 6-amino-2-hydroxypyridine sulphate (10·0 g.) in pyridine (60 c.c.) was added, with cooling, *p*-acetamidobenzenesulphonyl chloride (14·0 g.) at 60°. The resulting solution was heated on the steam-bath for 10 minutes; addition of water (500 c.c.) gave an oil which slowly solidified. The solid, after being washed with water, was crystallised from alcohol (charcoal), giving the above *ester* (10·1 g.; 67·5%) (Found : N, 13·5. $C_{13}H_{13}O_4N_3S$ requires N, 13·7%). Extraction of the charcoal with acetone (Soxhlet) gave 0·3 g. of 6-p-*acetamidobenzenesulphonamido-2-pyridyl* p-*acetamidobenzenesulphonate* (II), m. p. 222° after crystallisation from 50% acetic acid, which was better obtained as follows. To a solution of the ester (I) (25·2 g.) in pyridine (68 c.c.) was added *p*-acetamidobenzenesulphonyl chloride (20·4 g.). The solution became warm; after 30 minutes, water (800 c.c.) was added, followed by sufficient acetic acid to render the mixture acid to litmus. The gum which formed slowly hardened. The bulk (A) was used in the alkaline hydrolysis described below; a small amount crystallised from 70% alcohol in colourless needles, m. p. 222°, not depressed by admixture with the product from the first experiment. It was sparingly soluble in the ordinary organic solvents (Found : N, 11·0. $C_{21}H_{20}O_6N_4S_2$ requires N, 11·1%).

6-*Amino-2-pyridyl* p-*Aminobenzenesulphonate*.—Through a suspension of the corresponding acetyl compound (I) (2·0 g.) in dry alcohol (20 c.c.), dry hydrogen chloride was passed without

cooling. The mixture became hot and solution ensued, followed within a few minutes by precipitation of a crystalline solid. After 30 minutes, dry ether was added, and the presumed hydrochloride filtered off, washed with dry ether, and dissolved in water (30 c.c.). Ammonia precipitated the *ester*; it consisted of colourless needles, m. p. 148°, and was insoluble in cold dilute sodium hydroxide solution. It gave positive diazo-coupling reactions (Found: N, 15·9. $C_{11}H_{11}O_3N_3S$ requires N, 15·8%).

Action of Warm Dilute Sodium Hydroxide Solution on the Acetamidobenzenesulphonate (I).—The compound (4·5 g.) was dissolved in 2N-sodium hydroxide (45 c.c.) at 50°. After 30 minutes the mixture was neutralised with acetic acid and concentrated to low bulk in a vacuum. On cooling, 2·3 g. of sodium sulphanilate were obtained. The filtrate from this, on extraction with chloroform, gave 6-amino-2-hydroxypyridine as an oil (1·1 g.), which was identified as its dihydrochloride (Found: Cl, 38·9. Calc.: Cl, 38·8%).

Action of Sodium Hydroxide Solution on the Ester (II).—The ester obtained above (A) weighed 38 g. in the moist condition. The estimated dry weight was 32·8 g. (79·5% of the theoretical amount). The wet solid was refluxed for 1 hour with 2N-sodium hydroxide; acidification with acetic acid gave a precipitate of *6-hydroxy-2-(p-aminobenzenesulphonamido)-pyridine* (rectangular plates, m. p. 239—240°, not raised by recrystallisation from 50% acetic acid). The yield was 19 g. (94%) (Found: N, 15·7. $C_{11}H_{11}O_3N_3S$ requires N, 15·8%). The pyridylamide was readily soluble in cold dilute sodium hydroxide solution; it was unchanged by boiling with 25% sodium hydroxide solution for several hours, but after 10 minutes' boiling with 2N-hydrochloric acid, sodium sulphanilate was precipitated in 70% yield. Diazo-coupling tests were positive.

The thanks of the author are due to the Directors of Messrs. May and Baker, Ltd., for permission to publish the above observations.

RESEARCH LABORATORIES,
MESSRS. MAY AND BAKER, LTD., DAGENHAM. [*Received, March 31st*, 1941.]

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55. *Electrolytic Dissociation Processes. Part III. The Exchange of Radio-bromine between Inorganic and Organic Bromides.*

By FRED FAIRBROTHER.

The exchange of radio-bromine between a number of pairs of inorganic and organic bromides has been studied. With radioactive aluminium bromide the exchange generally reaches completion very quickly at room temperature, the notable exception being bromobenzene, with which the exchange is slow. Other inorganic bromides, *e.g.*, stannic bromide and antimony tribromide show less power of exchange and only exchange readily with the more easily ionisable organic bromides, *e.g.*, *tert.*-butyl bromide. The ease of exchange is correlated with the energy of formation of a metal complex ion and the ionisation potential of the organic radical.

IN a previous communication (J., 1937, 503) it was shown that the hydrogen chloride liberated in Friedel–Crafts reactions using aluminium chloride is in radioactive equilibrium with the latter, and also that an exchange of chlorine atoms takes place between the aluminium chloride and the organic chloride even in the absence of a third component. Experiments have now been carried out with a number of pairs of inorganic and organic bromides, which show that in many cases the exchange of bromine atoms is complete and rapid. The number of such possible combinations involving the variation of both the inorganic and the organic bromides is clearly very large. The present results, however, form a general survey of the problem and indicate the general nature of the exchange.

Radioactive aluminium bromide readily exchanges all its bromine atoms with those of most organic bromides when simply dissolved in the latter, or when both reactants are dissolved in carbon disulphide; this exchange occurs with great rapidity at room temperature. The only exception found was bromobenzene, with which the exchange with aluminium bromide is very slow.

Stannic bromide is less able to exchange its bromine atoms. It exchanges slowly, but

with measurable speed, with *tert.*-butyl bromide and benzyl bromide, but shows no exchange under similar conditions with ethyl bromide. It forms a very convenient reagent for the introduction of radio-bromine into *tert.*-butyl bromide, which undergoes rapid decomposition in the presence of aluminium bromide.

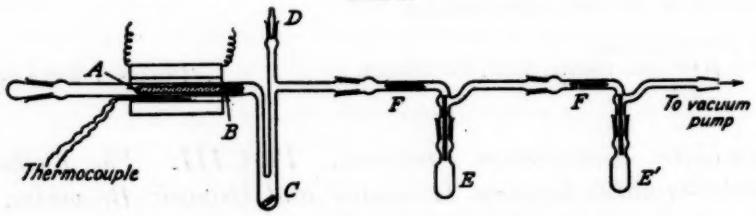
Other inorganic bromides, such as antimonious, auric, zinc, cupric, mercuric, and indium bromides, were also found to possess more or less power of exchange with certain classes of organic bromides, but no exchange was observed with potassium, calcium, or phosphorous bromide.

Brejneva, Roginsky, and Schilinsky (*Acta Physicochim. U.R.S.S.*, 1936, **5**, 549), in an investigation on the possibilities of the introduction of radioactive halogens into organic molecules, report the radioactive exchange between aluminium bromide and a number of organic bromides. They used a different technique from that used in the present work, with which on the whole their results are in agreement. They state, however, that benzyl bromide will exchange its bromine with aluminium bromide, whereas if these two substances be brought together, even in the presence of considerable carbon disulphide as diluent, there is an immediate condensation to a red solid and a vigorous evolution of hydrogen bromide.

Experimental.

The radio-bromine was prepared by irradiating about 5 kg. of ethylene dibromide with a 200-mc. radium–beryllium source of neutrons placed in the centre, the containing vessel being surrounded by an average of about 15 cm. radial thickness of paraffin wax. The irradiation was

Fig. 1.



carried out overnight or over several days, after which the radio-bromine was extracted by shaking with an aqueous solution of 1 g. of potassium bromide. The bromide was next precipitated as silver bromide, which was quickly washed and dried; an exception to this was made in the case of active mercuric bromide, which was prepared directly from the potassium bromide by the addition of a solution of mercuric acetate and cooling in ice, the mercuric bromide being only slightly soluble at 0°. In all other cases the active silver bromide was used as an intermediate product.

Aluminium bromide. This was prepared, and its exchange experiments carried out, in the apparatus shown in Fig. 1, which was made of Pyrex glass throughout, the ground joints being made vacuum-tight with picein wax. The active silver bromide was intimately mixed with about three times its weight of cleaned aluminium filings, placed in a hard-glass tube *A*, and kept in position by a loose plug of glass wool. This tube was then placed in the outer tube *B*, and the apparatus closed and evacuated to a few μ mm. of mercury. *B* was then gently heated externally by a small electric furnace; at about 450° the reaction $2Al + 6AgBr^* = Al_2Br^*_6 + 6Ag$ occurred rapidly but smoothly, and the $Al_2Br^*_6$ volatilised on to the cool part of the tube. From thence, by manipulation of a small gas burner, it was volatilised into the cooled exchange vessel *C*. The final product was quite white. The use of aluminium filings was found to be necessary as the reaction with aluminium powder was too violent and ejected the reaction mixture into the exchange vessel. The entire apparatus as shown in Fig. 1 was dismantled and cleaned before each experiment.

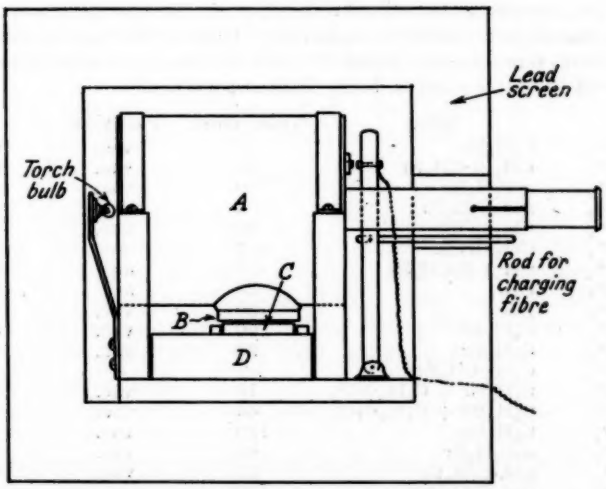
On completion of the preparation of the active aluminium bromide, *A* and *B* were cooled, and dry air admitted into the apparatus. The stopper *D* was then removed for a few moments, and the liquid bromide, alone or in carbon disulphide solution, added through a long capillary thistle funnel. A small pellet of iron enclosed in a glass tube and operated by a magnet, served to stir the contents of *C*.

At the end of the time allowed for the exchange, one of two methods was used for the partition of the aluminium bromide from its reaction partner: (*a*) the organic bromide was quickly

volatilised in a vacuum at room temperature and condensed in the receiver *E*, which was cooled in liquid air or in carbon dioxide–acetone. A 7-cm. plug of glass wool *F* prevented any transfer of solution into the receiver by spray or bumping. This method of partition was used especially for the more volatile and the easily hydrolysed bromides, and is designated below as " vac." When the aluminium bromide was used to prepare a radioactive organic bromide for experiments with a second inorganic bromide, the latter was placed in *E*, which then became the reaction vessel, and the partition was brought about by volatilisation into a second receiver *E'*. The alternative method of partition, (*b*), consisted in removing the contents of *C* by suction through a capillary tube and transferring them below the surface of dilute nitric acid (about 1·5M) in which the aluminium bromide was immediately decomposed; the organic component was then extracted by ether. A control experiment showed that no exchange of Br^- with the organic bromide occurred during the time required for these operations. This method of partition is designated as " aq."

Stannic bromide. This was prepared and used in an apparatus similar to the above, but with a somewhat narrower tube *B*, which was filled with fairly coarse tin powder (prepared by vigorously stirring molten tin whilst it cooled) and heated to about 150°. The $AgBr^*$ was gently warmed with a mixture of potassium dichromate and sulphuric acid in a small flask, and the liberated bromine led over the tin in a stream of dry nitrogen. The initial stage of the reaction

FIG. 2.



between fresh tin and bromine is slow and care was required to secure the reaction of all the bromine; a charge of tin powder which had already been treated with bromine, and freed from moisture by a preliminary drying in the nitrogen stream, reacted more readily. The samples of $SnBr^*_4$ were quite white and free from excess bromine. For convenience in handling, the active $SnBr^*_4$ was in some cases diluted by the addition of about 1 g. of pure inactive $SnBr_4$.

With the exception of $HgBr^*_2$, all the other inorganic bromides were used in the inactive state, exchanges being carried out with organic bromides in which the radio-bromine had been introduced by aluminium bromide or stannic bromide. In the case of antimony tribromide a 10% Rochelle salt solution was used for the aqueous partition, to prevent precipitation of antimonious oxide.

In all cases, on completion of the partition, the bromine in the two compounds was converted by appropriate methods into silver bromide, from the activity of which the specific activities of the bromines concerned in the exchange were calculated. The activity of the silver bromide specimens was measured as follows. A Lauritsen quartz-fibre electroscope (*Rev. Sci. Instr.*, 1937, **8**, 438) was mounted in a copper ionisation chamber (*A*, Fig. 2) of about 1-litre capacity, lagged with felt to prevent sudden temperature changes, and provided on the under side with a thin aluminium foil window *B*, of about 3 mg./sq. cm. A weighed amount (0·5—1·0 g.) of the radioactive silver bromide was placed in a 5-cm. Petri dish *C*, which fitted in a shallow cavity in a horizontal wooden slide *D*, by which it could be placed in accurate registration immediately underneath the aluminium window.

The electroscope was mounted inside a 5-cm. thick lead screen, which reduced the natural background drift to about half that of the unscreened electroscope. This background was frequently measured and remained very constant, about 0·16 division per min., for most of the experiments. The activities of the samples measured, except where no exchange had occurred, were always much greater than the background, usually by more than 10—100 times. The correction for the self-absorption of the radiation by the silver bromide was estimated by observing the reduction in activity on interposing a series of aluminium foils between the silver bromide and the electroscope, and extrapolating to zero absorber. This correction amounted to about 10% per g. of silver bromide in the dish and any uncertainty was minimised by taking approximately equal quantities of AgBr* for each measurement. Apart from measurements involving the selective extraction of the 18-min. period of ^{80}Br, little correction was required for the decay of the activity of the specimens during measurement, as the latter was usually carried out after the 18-min. period had disappeared, and required a time which was short compared with the half-life of the 4·5-hr. period. The estimated overall precision of the measurements was about ± 5—10% of the total activity of each specimen; a recorded exchange of only a few units % in the following table is regarded as outside the experimental error.

The results of the exchange experiments are summarised in the table, in which the reactants are given as MBr and RBr respectively, the radioactive component being marked with an asterisk, thus—$Al_2Br^*_6$. The times of contact of the reactants are given in minutes and r, the "ratio of activities," indicates the ratio of the specific activity of the initially inactive bromine to that of the initially radioactive bromine, at the time of partition: a ratio approaching unity indicates therefore a complete exchange. Unless otherwise indicated, all exchanges were carried out at room temperature (about 15°) and the reactants were mixed together without solvent, in the case of insoluble solutes, being shaken together.

MBr.	RBr.	Time, mins.	Partition.	r.
$Al_2Br^*_6$	C_2H_5Br	5	vac.	0·90
$Al_2Br^*_6$	$CH_2Br{\cdot}CH_2Br$	20	vac.	0·97
$Al_2Br^*_6$	*n*-C_4H_9Br	10	vac.	0·97
$Al_2Br^*_6$	*tert.*-C_4H_9Br	5	vac.	1·0
$Al_2Br^*_6$	$CH_3{\cdot}COBr$	20	vac.	0·80
$Al_2Br^*_6$	$CH_2{:}CHBr$	<2	vac.	0·97 [1]
$Al_2Br^*_6$	$CH_2{:}CH{\cdot}CH_2Br$	<2	aq.	0·84 [2]
$Al_2Br^*_6$	CBr_4	20	aq.	0·89 [3]
$Al_2Br^*_6$	PBr_3	30	vac.	0·98
$Al_2Br^*_6$	C_6H_5Br	90	vac.	0·03 [4]
$Al_2Br^*_6$	C_6H_5Br	90	vac.	0·82 [5]
$Al_2Br^*_6$	$C_6H_5{\cdot}CH_2Br$	—	—	— [6]
$Al_2Br^*_6$	$C_2H_5Br + C_6H_5{\cdot}NO_2$	10	vac.	0·025
$Al_2Br^*_6$	$C_2H_5Br + C_6H_5{\cdot}NO_2$	40	vac.	0·075
$SnBr^*_4$	C_2H_5Br	120	vac.	<0·01
$SnBr^*_4$	*n*-C_4H_9Br	60	vac.	0·12
$SnBr^*_4$	*tert.*-C_4H_9Br	15	vac.	0·10
$SnBr^*_4$	*tert.*-C_4H_9Br	150	vac.	0·92
$SnBr^*_4$	$CH_3{\cdot}COBr$	25	vac.	0·62
$SnBr^*_4$	$CH_2{:}CH{\cdot}CH_2Br$	30	vac.	0·02
$SnBr^*_4$	$C_6H_5{\cdot}CH_2Br$	150	vac.	1·05
Au_2Br_6	$C_2H_5Br^*$	30	vac.	++ [7]
Au_2Br_6	*tert.*-$C_4H_9Br^*$	30	vac.	0·74 [8]
$SbBr_3$	*tert.*-$C_4H_9Br^*$	30	ac.	1·0
$SbBr_3$	$C_2H_5Br^*$	100	vac.	—
$SbBr_3$	$CH_2Br{\cdot}CH_2Br^*$	120	aq.	—
$SbBr_3$	$CH_2Br{\cdot}CH_2Br^*$	120	aq.	0·20 [9]
$HgBr_2$	$C_2H_5Br^*$	5	vac.	—
$HgBr_2$	*tert.*-C_4H_9Br	100	vac.	+
$HgBr^*_2$	$C_6H_5{\cdot}CH_2Br$	30	vac.	+
$ZnBr_2$	*tert.*-$C_4H_9Br^*$	90	vac.	+
$CuBr_2$	*tert.*-$C_4H_9Br^*$	90	vac.	+
$AsBr_3$	$C_2H_5Br^*$	10	vac.	—
PBr_5	$C_2H_5Br^*$	120	vac.	—
$InBr_3$	*tert.*-$C_4H_9Br^*$	30	vac.	+
$InBr_3$	$C_2H_5Br^*$	30	vac.	+
KBr	$C_2H_5Br^*$	15	vac.	—
$CaBr_2$	*tert.*-$C_4H_9Br^*$	60	vac.	—

[1] Exchange at 0°: some polymerisation and charring. [2] 5% Allyl bromide solution in CS_2. [3] 10% CBr_4 solution in CS_2. [4] Room temp. [5] 100°. [6] Instantaneous condensation with evolution of HBr. [7] Solubility small but considerable exchange. [8] In 50% solution in ether. [9] Refluxed: b. p. 132°.

All the organic bromides examined, with the exception of bromobenzene, very readily exchanged their bromine atoms with those of aluminium bromide. With bromobenzene, the exchange only occurs easily at higher temperatures. The dissolution of the aluminium bromide in nitrobenzene, in the proportion of about 1 mol. in 2½ mols., effected a very large reduction in the rate of exchange with ethyl bromide. This may readily be attributed to the formation of the double compound between the nitrobenzene and the aluminium bromide, with a consequent reduction in the equilibrium concentration of the latter in the system.

Stannic bromide and antimony tribromide possess less power of exchange than aluminium bromide, and at room temperature are only able to exchange their bromine atoms with those of the more reactive organic bromides. The small exchange between stannic bromide and allyl bromide was unexpected in view of the reactivity of the latter, but repeated experiments confirmed that this exchange occurs very slowly at room temperature.

Auric bromide, though of limited solubility, appears to possess considerable exchange ability. This is not surprising in view of the similarity between its dimeric formula and that of aluminium bromide.

The exchange results marked + refer to systems in which the solubility of the inorganic bromide was too small to permit of the quantitative measurement of the exchange. In these cases the exchange was confirmed by the presence of the 4·5-hr. period of ^{80}Br. It has already been observed (Fairbrother, *Nature*, 1939, **145**, 307) that many inorganic bromides will extract the 18-min. period of radio-bromine from active ethyl bromide. Probably any inactive inorganic bromide when shaken with any active organic bromide would show some radioactivity after separation: it is only when all the radio-bromine isotopes are transferred that a true exchange can be considered to have occurred. This in fact provides a convenient qualitative test of exchange, especially for insoluble inorganic bromides: a decay of the activity of the latter after separation with a pure half-life of 18 mins. and no " tail " indicates that no chemical exchange of the bromine atoms has occurred. Such results are indicated in the table by the — sign.

Discussion.

In the previous communication (*loc. cit.*) it was suggested that the radioactive exchange took place through the formation of a carbonium ion and a complex metal halide ion, *e.g.*, $2RBr + Al_2Br_6 \rightleftarrows 2R^+ + 2[AlBr_4]^-$. A similar mechanism has been postulated by Bodendorf and Böhme (*Annalen*, 1935, **516**, 1) to account for the catalytic racemisation of α-phenylethyl chloride by inorganic chlorides. In certain circumstances, as shown by Wohl and Wertyporoch (*Ber.*, 1931, **64**, 1357, 1369), it is actually possible for a weakly conducting system to be formed.

It is not necessary, however, for complete radioactive exchange to take place, that the equilibrium concentration of the carbonium ion–metal complex ion pair should be large. Indeed, a consideration of the energies involved in the change $RBr + MBr_n \longrightarrow R^+ + [MBr_{n+1}]^-$ makes it appear probable that in many cases the net results would be a gain in free energy in the forward direction, and that therefore only a small equilibrium concentration of the carbonium ion will be formed, which may be quite undetectable by cryoscopic, ebullioscopic, or conductivity methods. Moreover, if a large concentration of carbonium ion were formed, there would be much decomposition with the liberation of hydrogen bromide and formation of olefin. This was observed in certain cases, notably with *tert.*-butyl bromide and aluminium bromide, and it has long been known that the action of aluminium chloride on aliphatic chlorides may give rise to olefins (Kerez, *Annalen*, 1885, **231**, 306; Monneyrat, *Ann. Chim.*, 1900, **20**, 530). Also, Ingold and his collaborators have shown (J., 1937, 1271) that olefin elimination accompanies those cases of halide hydrolysis in which the rate-controlling mechanism is halogen ionisation, *i.e.*, the formation of a carbonium ion.

The ionisation process may be represented by a cycle. In the case of aluminium bromide, which can be regarded as $AlBr_3$, since it is present in this form to some extent in many solvents and largely so in ethyl bromide (Wertyporoch, *Ber.*, 1931, **64**, 1371), the cycle would be

$$\begin{array}{ccc} RBr + AlBr_3 & \xrightarrow{+\,D_{C-Br}} & R + Br + AlBr_3 \\ {\scriptstyle \Delta S + \Delta H}\downarrow & & \downarrow{\scriptstyle +\,I_R - E_{Br}} \\ R^+ + [AlBr]_4^- & \xleftarrow[-\,Q_{[AlBr_4]^-}]{} & R^+ + Br^- + AlBr_3 \end{array}$$

in which ΔH is the algebraic sum of D_{C-Br}, the C–Br bond energy, I_R, the ionisation potential of the free radical R, E_{Br}, the electron affinity of the bromine atom, and $Q_{[AlBr_4]^-}$, the energy of formation of $[AlBr_4]^-$ from $AlBr_3$ and Br^-. Since the process takes place in solution, to these must be added ΔS, the net change in solvation energies.

A consideration of these various magnitudes leads to the conclusion that the major factor determining the exchange process with a given inorganic halide is I_R; if a number of different metal halides are under review, the energy of formation of the complex metal ion is also a major factor.

Thermal and other data show that the bond energies of organic halides do not vary greatly with different organic radicals. For example, Butler and Polanyi (*Nature*, 1940, **146**, 129) suggest bond energies for a number of iodides which only vary by 8·9 kg.-cals./mol. between phenyl and *tert.*-butyl: one may expect a similar range to be found in the case of the bromides, with an average value of about 60 kg.-cals./mol. Any variation in the net solvation energy changes in the cases at present under consideration would also be too small to account for the observed variation in ease of bromine exchange.

Of the values of the other factors involved, the only one which is known with any certainty is E_{Br}, which may be taken as 81·5 kg.-cals./mol. (Mayer and Helmholz, *Z. Physik*, 1932, **75**, 19).

Klemm and Jacobi (*Z. anorg. Chem.*, 1932, **207**, 186) give the heat of formation of aluminium bromide as $Al + 3Br_{(liq.)} \longrightarrow AlBr_{3\,(solid)} + 121$ kg.-cals., and Fischer and Ralphs (*ibid.*, 1932, **205**, 1) calculate the heat of the reaction $Al_2Br_6 \longrightarrow 2AlBr_3$ as $-26{\cdot}5$ kg.-cals. and the heat of volatilisation of Al_2Br_6 as 12·1 kg.-cals./mol. From these data and the heats of volatilisation of aluminium and dissociation of bromine molecules, it appears that the strength of each Al–Br bond in $AlBr_3$ is about 70 kg.-cals. This may be taken as the lower limit of formation of a fourth Al–Br bond, *i.e.*, of the formation of $[AlBr_4]^-$ from $AlBr_3$ and Br^-. The actual energy of formation may be somewhat greater than this on account of increased resonance in the ion, but it does not seem probable that it can be much greater than about 100 kg.-cals./mol. The energy of formation of a complex anion will be less in the case of the other inorganic bromides used.

The greatest uncertainty lies in the value of I_R. Only very few organic radicals have been studied in this connexion, and the values given for the ionisation potentials vary between wide limits. For example, for the methyl radical, Fraser and Jewitt (*Proc. Roy. Soc.*, 1937, *A*, **160**, 563), using a molecular beam technique, found $11{\cdot}2 \pm 0{\cdot}8$ volts, and for the ethyl radical, $10{\cdot}6 \pm 0{\cdot}8$ volts. On the other hand, Baughan, Evans, and Polanyi (private communication) conclude from chemical evidence that the ionisation potential of the methyl radical is about 7·8 volts (180 kg.-cals./mol.). Other estimates by physical and theoretical methods lie between these.

It appears, however, even within the probable limits of the values of these various factors, that the ionisation of an organic bromide by an inorganic bromide may often be an endothermic process. This supposition is borne out by the low conductivities of such solutions (cf. Wertyporoch, *loc. cit.*), which is indicative of a small equilibrium concentration of free ions. It is possible that a greater concentration of undissociated ion-pairs may be present, especially in view of the fairly low dielectric constants of most of the liquids. An answer to this question is being sought through the measurement of the dielectric polarisabilities of mixed solutions of organic and inorganic halides, which should show an increase of polarisability if there is any appreciable formation of ion-pairs.

The effect of temperature on the exchanges between aluminium bromide and bromobenzene and between antimony tribromide and ethylene dibromide shows that these exchanges possess an activation energy. This is probably general, and is in accord with the observations of other authors that various inorganic halide catalysts can be used in the Friedel–Crafts syntheses, but require higher temperatures than aluminium halides; *e.g.*, Menschutkin (*J. Russ. Phys. Chem. Soc.*, 1913, **45**, 1710) in the case of antimony trichloride and Bredereck *et al.* (*Ber.*, 1939, **72**, 1414) in that of beryllium chloride.

It is to be expected that a similar effect will be observed in the corresponding radioactive exchanges. The study of the rates of halogen exchange over a range of temperatures, between various pairs of organic and inorganic bromides, and the evaluation of the activ-

ation energies of the process, offer a chemical method of comparing the ionisation potentials of different organic radicals and also of discriminating quantitatively between the potential catalytic properties of various inorganic bromides. In view of the more general use of chloride catalysts, a similar study of the exchange between organic and inorganic chlorides would be desirable, since it is not possible in all cases to extrapolate from the bromide to the chloride. This was not possible with the present technique, since irradiation of a chloride in the same manner leads only to a very weak product of radio-chlorine, which moreover has a relatively short half-life (37 mins.). Such experiments could be carried out by activation of the chloride by high-velocity deuteron bombardment, as with aluminium chloride in Part II of this series (J., 1937, 503).

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MANCHESTER UNIVERSITY. [*Received, March 31st*, 1941.]

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56. *Molecular Volume and Structure. Parts I and II.*

By T. W. GIBLING.

Part I.

The bases of the method in general use for the calculation of parachors are discussed, and it is suggested that atomic and structural equivalents should be replaced by group values. The difference in parachor corresponding to addition of a CH_2 group appears to show regular progressive increase throughout any homologous series of compounds, except among the earlier members, in the volumes of which decreases due to " interference effects " are always found. The parachors of the normal paraffins, $CH_3{\cdot}[CH_2]_{n-2}{\cdot}CH_3$, can be expressed as $[2c + (n - 2)k]f^n$, where c, k, and f are constants; $2c + (n - 2)k$ is taken as the standard value for the parachor. Standard values are allotted to the different groups found in the molecules of paraffins and olefins, and certain " interference reductions " are assessed. The new method gives satisfactory agreement (of the order of 0·2%) between calculated and mean observed values, and also leads to the better elucidation of problems of structure, as will be shown in subsequent parts of this series.

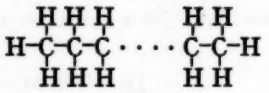
THE application of molecular volumes to problems of structure must be limited to a large extent by the methods employed in the analysis of these quite complex functions, and undue simplification in treatment will tend to impair their usefulness.

The most successful of the attempts to devise comparable conditions for the measurements of molecular volumes had a purely empirical origin. MacLeod (*Trans. Faraday Soc.*, 1923, **19**, 38) found that the surface tension (γ) of a normal liquid was proportional to the fourth power of the difference between its density (D) and that of its saturated vapour (d) at all temperatures from its freezing point to about 30° below its critical temperature; *i.e.*, $\gamma^{\frac{1}{4}}/(D-d) = C$ (a constant). Sugden (J., 1924, **125**, 1177) multiplied the above expression by the molecular weight (M) and called the product the " parachor " of the liquid: $[P] = M\gamma^{\frac{1}{4}}/(D - d)$. He showed that the parachor could be regarded, at any rate to a first approximation, as the molecular volume of a liquid under standard internal pressure, and that the function possessed the property of additivity to a remarkable degree. His method of analysis, based largely upon that of Kopp (*Annalen*, 1855, **95**, 153, 303) for molecular volumes of liquids at the boiling point, was attractively simple but had certain shortcomings, as was realised by Mumford and Phillips (J., 1928, 155; 1929, 2112; *Ber.*, 1930, **63**, 1818), whose proposed modifications, however, did not gain general acceptance.

In recent years improvement in technique has led to some advance in the accuracy of parachor determination; *e.g.*, Gillespie, Macbeth, and Mills (J., 1940, 280) estimate the normal maximum error in their parachor measurements to be less than 1 in 4000, as compared with Sugden's 1 in 200. Some workers (*e.g.*, Vogel, J., 1938, 1323; 1940, 1528)

have been obliged to postpone comparison of experimental with calculated results until a more satisfactory method of evaluating the necessary constants can be evolved. The present paper is an attempt to derive such a method on the assumption that the parachor, possibly in a slightly modified form, may be regarded as a truly additive and constitutive function capable of affording considerably more information regarding the structure of molecules than has hitherto been realised.

In his calculation of " atomic constants," Sugden (" The Parachor and Valency," 1929, 35) tacitly assumed that the contribution of any atom to the molecular volume is the same no matter to what other atoms it may be united by single bonds, *e.g.*, that in (I) the effective volumes of the carbon and hydrogen atoms are constants. It can be regarded as axiomatic



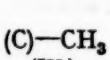
(I.)

(II.)

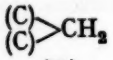
(III.)

that the volume contribution of a given atom will vary with the nature of the atoms to which it is linked, and it is not legitimate to assume that the extent of such variation is negligible, especially in the case of carbon and hydrogen, the dimensions of which differ considerably. In the molecule (I) there are two types of carbon atom, the two end atoms differing from the others, and it is unlikely that the two types will contribute equally to the volume.

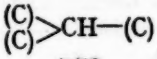
Sugden's method of calculation also made no allowance for the "interference" which is bound to occur when atoms, though not directly united, are nevertheless brought into fairly close conjunction, as in such groupings as (II) and (III), and it ignored the fact that the parachors recorded for compounds containing branched carbon chains are, in the majority of cases, substantially smaller than those of their so-called straight-chain isomers. Mumford and Phillips realised that a definite contraction, as measured by parachor value, is to be associated with a change in structure from (V) to (VI), and that a further contraction is observable in a change from (VI) to (VII), but they failed to appreciate the corollary that the change in structure from (IV) to (V) should also involve reduction of volume. They suggested the adoption of negative parachor equivalents, or " strain



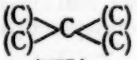
(IV.)



(V.)



(VI.)



(VII.)

constants," to allow for diminution of volume " brought about either by the closer packing of atoms or groups within the molecule, or by a decrease in the effective size of one or other of the atoms concerned," and they also recognised the variability of effective atomic parachors, suggesting the use of different values for hydrogen according to the nature of the atom with which it is united. They did not, however, make full application of these principles to their fundamental calculation, the determination of constants for carbon and hydrogen in the paraffins.

No satisfactory method of measuring an " atomic volume " of any kind has yet been evolved, except, of course, for helium, neon, etc., and for certain elements in the solid state, and indeed, it is doubtful whether any precise significance can be attached to the term as applied to liquid compounds. In these circumstances it seems better to calculate " group values ", *i.e.*, the normal contributions of (IV), (V), etc., to the molecular volumes under consideration, and to attempt to assess any " interference corrections " which may be required owing to the proximity of other atoms or groups in the molecules.

There is first, however, a further difficulty to be resolved. The abnormally large parachors recorded for substances of high molecular weight have not yet received a satisfactory explanation. They have been ascribed to experimental error, but careful examination of all homologous series in which members sufficiently far apart have been investigated indicates that the " expansion effect " is quite general, the CH_2 difference slowly but steadily increasing with increase in the parachor values. This " expansion " partly explains the

difficulty of deciding upon a satisfactory value for the CH_2 equivalent. Sugden's original number, 39·0, was a mean derived from the parachors of members of several homologous series, including compounds whose molecules are "associated" in the liquid state and others with groups of strongly polar character which cause considerable reductions in the parachors of the earlier members in the series, as is shown in Part II. Moreover, no distinction was made between normal compounds and those having branched chains, and values recorded for the parachors of isomerides were averaged, all alkyl esters of fatty acids, for example, being treated as one series. Mumford and Phillips's value, 40·0, is more satisfactory, being approximately the mean derived from the observed parachors from ethane to decane; whereas that of Vogel (J., 1934, 1758), *viz.*, 40·3, takes into account the parachors of substances of higher molecular weight.

In "A List of Parachors" (*Brit. Assoc. Rep.*, 1932, 265), besides the eight values lying between 1000 and 2500 (all of which are treated in Parts I and II), some dozen values of between 500 and 1000 are given for compounds of fairly simple type (or at least 20 if the higher fatty acids are correctly treated as consisting mainly of dimeric molecules) and, in all cases where it is possible to make a comparison, the parachors recorded are appreciably greater than those calculated by using mean "group values" and applying the necessary "interference corrections." For the great majority of substances with parachors of less than 500 the differences to be expected lie within the limits of experimental error, but even here a comprehensive investigation shows that, the mean "group values" being used, the parachors calculated for the lower or higher members in the various series are respectively, on the whole, rather greater or less than the experimental values. The necessity for postulating this expansion effect is made especially clear in the series of esters, tricaprin to tristearin, with parachors (between 1400 and 2400) which agree almost perfectly with the calculated values (p. 308). If the expansion effect were ignored, the whole argument with regard to the structure of the molecules—an argument immediately confirmed by the parachors (about 200—830) of alkyl carbonates and malonates—would fall to the ground. It is perhaps of some significance that an exactly similar effect is apparent in molecular volumes of liquids at the boiling point, though in this case the rate of expansion is considerably greater. Whatever may be the physical cause of the expansion phenomenon, there can be little doubt of its existence. Assuming then the desirability of arriving at a function that shall be as nearly as possible perfectly additive (as well as, to some extent, constitutive), one must apply some slight correction to the parachor as at present defined.

The author suggests that examination of the parachors of any sufficiently extended homologous series will show that the CH_2 difference is not constant, but increases progressively (though very slowly at first) from member to member, *any definite irregularities observed in the progression being traceable to peculiarities in structure.*

Among the normal paraffins, $CH_3{\cdot}[CH_2]_{n-2}{\cdot}CH_3$, the increase occurs with perfect regularity from the *second* member onwards, and the parachors of these compounds may be represented with considerable accuracy by the formula $[2c + (n - 2)k]f^n$, in which c and k are the effective contributions by CH_3- and $-CH_2-$, respectively, and f is an "expansion factor" only slightly greater than unity. Using the following values for the constants: $c = 55{\cdot}2$, $k = 39{\cdot}8$, $f = 1{\cdot}0004165$, one finds that the percentage differences between the mean observed parachors and the calculated values for all the n-paraffins investigated lie between $-0{\cdot}2$ and $+0{\cdot}5$.

Normal paraffins, C_nH_{2n+2}.

n.	[P], calc.	[P], obs.	Mean diff., %.	n.	[P], calc.	[P], obs.	Mean diff., %.
2	110·5	110·5	±0·0	8	350·4	350·3, 351·0	+0·1
3	150·4	150·8	+0·3	10	430·6	429·7	−0·2
4	190·3	190·3	±0·0	26	1077	1082	+0·5
6	270·3	270·1, 270·4, 270·4, 273·3	+0·3	32	1322	1322	±0·0
				60	2480	2480	±0·0
7	310·3	309·3, 310·8	−0·2				

The agreement is usually within 0·2%, which is about the order of accuracy to be expected in parachor determinations, and this may be compared with that obtained by using the various "atomic constants" previously proposed and making no correction for expansion:

Sugden (S), C, 4·8, H, 17·1; Mumford and Phillips (MP), C, 9·2, H, 15·4; Vogel (V), C, 11·5, H, 14·4.

Mean difference, %, between [P] obs. and [P] calc.

n.	S.	MP.	V.	*n*.	S.	MP.	V.
2	−1·5	+0·3	+1·0	8	+1·3	+0·0	−0·2
3	−0·3	±0·0	+0·7	10	+1·3	−0·3	−0·5
4	−0·1	−0·3	+0·2	26	+3·2	+1·3	+0·5
6	+1·1	−0·2	+0·2	32	+3·1	+0·8	+0·3
7	+0·9	−0·2	−0·3	60	+4·5	+2·0	+1·4
					Mean 1·7	0·5	0·5

Investigation of other homologous series shows that expansion occurs at exactly the same rate as in the *n*-paraffins; *i.e.*, the magnitude of the CH_2 increment depends upon the magnitude of the parachors, but is independent of the type of compound. Thus the set of corrections which can readily be prepared for the *n*-paraffins (see Conversion Table, p. 304) may be graphed and used for correcting the observed parachors of other substances. The corrected values so obtained are found to be, within the limits of experimental error, truly additive (and constitutive) functions and may be styled "Standard Values" (S.V.). Conversely, using the effective group values previously determined and applying any interference corrections that may be necessary, one can convert the S.V. so calculated for any member in a series into the (calculated) parachor, and the value obtained may be compared with the experimental value. The S.V. of a *n*-paraffin from ethane onwards is $2c + (n-2)k$, and the parachor is this value multiplied by f^n; the difference between the two is, of course, the "expansion correction" (E.C.).

The method of calculation, using normal group values (already corrected for interference effects), may be illustrated in the case of *n*-pentane:

$2CH_3{\cdot}(C)$ at $55{\cdot}2 = 110{\cdot}4$ } S.V., calc. = 229·8; add E.C. = 0·5;
$3(C){\cdot}CH_2{\cdot}(C)$ at $39{\cdot}8 = 119{\cdot}4$ } then $[P] = 230{\cdot}3$.

From the parachors recorded for *iso*- and *neo*-paraffins, S.V. for the groupings (VI) and (VII) have been determined, with the result that the values for groups occurring in paraffins are found to be as follows:

Group.	S.V.	Diff.	Group.	S.V.	Diff.
(IV)	55·2	—	(VI)	22·2	−17·6
(V)	39·8	−15·4	(VII)	2·4	−19·8

The constant increase in these differences must be due to interference between atoms attached to a common carbon atom. Assuming, as would appear most likely, that the hydrogen atoms are too small to produce an appreciable interference effect, one sees that the reduction in parachor value due to the grouping (II) is 2·2. Hence:

Group.	Ideal S.V. (without interference).	Constant diff.	Group.	Ideal S.V. (without interference).	Constant diff.
(IV)	55·2	—	(VI) *	28·8	−13·2
(V)	42·0	−13·2	(VII) †	15·6	−13·2

* This obviously involves three $C<\begin{smallmatrix}C\\C\end{smallmatrix}$ groupings.

† In $\begin{smallmatrix}C_1\\C_2\end{smallmatrix}>C<\begin{smallmatrix}C_3\\C_4\end{smallmatrix}$ there are 6 interference effects to be considered: those between C_1, C_2; C_1, C_3; C_1, C_4; C_2, C_3; C_2, C_4; and C_3, C_4.

From the parachors of olefins the following values are obtained:

Group.	S.V.	Diff.	Group.	S.V.	Diff.
$CH_2{=}(C)$	49·7	—	$\begin{smallmatrix}(C)\\(C)\end{smallmatrix}>C{=}(C)$	16·7	−17·6
$(C){\cdot}CH{=}(C)$	34·3	−15·4			

Thus the grouping $C<\begin{smallmatrix}C\\C\end{smallmatrix}$ appears to involve the same reduction in parachor as $C<\begin{smallmatrix}C\\C\end{smallmatrix}$, *viz.*,

2·2, and the following will therefore be the ideal values for the double-bonded groups found in olefins:

Group.	Ideal S.V. (without interference).	Constant diff.	Group.	Ideal S.V. (without interference).	Constant diff.
$CH_2=(C)$	49·7	—	$\begin{matrix}(C)\\(C)\end{matrix}\!>\!C=(C)$ *	23·3	−13·2
$(C)\cdot CH=(C)$	36·5	−13·2			

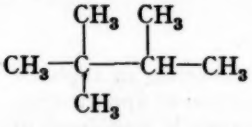
* This involves one $C\!<\!\begin{matrix}C\\C\end{matrix}$ and two $C\!<\!\begin{matrix}C\\C\end{matrix}$ groupings.

The following table gives the calculated and observed parachors for all paraffins and olefins included in the British Association list (see p. 301). The group values used in the calculations are as follows:

$CH_3\cdot(C)$, 55·2; $(C)\cdot CH_2\cdot(C)$, 39·8; $\begin{matrix}(C)\\(C)\end{matrix}\!>\!CH\cdot(C)$, 22·2; $\begin{matrix}(C)\\(C)\end{matrix}\!>\!C\!<\!\begin{matrix}(C)\\(C)\end{matrix}$, 2·4; $CH_2=(C)$, 49·7; $(C)\cdot CH=(C)$, 34·3; $\begin{matrix}(C)\\(C)\end{matrix}\!>\!C=(C)$, 16·7.

The method of calculation is shown in the following examples:

ββγ-Trimethylbutane



$5CH_3\cdot(C)$	at 55·2	= 276·0
$\begin{matrix}(C)\\(C)\end{matrix}\!>\!CH\cdot(C)$	at 22·2	= 22·0
$\begin{matrix}(C)\\(C)\end{matrix}\!>\!C\!<\!\begin{matrix}(C)\\(C)\end{matrix}$	at 2·4	= 2·4

S.V., calc. = 300·6
E.C.* = +0·8
∴ [*P*], calc. = 301·4

* E.C. is derived from a table of corrections constructed for the *n*-paraffins (see p. 301) or from a graph made from that table.

β-*iso*Amylene $CH_3\cdot CH=C\!<\!\begin{matrix}CH_3\\CH_3\end{matrix}$

$3CH_3\cdot(C)$	at 55·2 =	165·6
$(C)\cdot CH=(C)$	at 34·3 =	34·3
$(C)=C\!<\!\begin{matrix}(C)\\(C)\end{matrix}$	at 16·7 =	16·7

S.V., calc. = 216·6
E.C. = +0·4
∴ [*P*], calc. = 217·0

Hydrocarbon.	S.V., calc.	E.C.	[*P*], calc.	[*P*], obs.	Mean diff., %.
Ethane	110·4	+ 0·1	110·5	110·5	±0·0
Propane	150·2	+ 0·2	150·4	150·8	+0·3
Butane	190·0	+ 0·3	190·3	190·3	±0·0
*iso*Pentane	227·6	+ 0·5	228·1	230·0	+0·8
Hexane	269·6	+ 0·7	270·3	270·1, 270·4, 270·4, 273·3	+0·3
Heptane	309·4	+ 0·9	310·3	309·3, 310·8	−0·2
γ-Methylhexane	307·2	+ 0·9	308·1	306·6	−0·5
ββ-Dimethylpentane	305·0	+ 0·9	305·9	305·5	−0·1
ββ-Dimethylpentane	302·8	+ 0·9	303·7	305·3	+0·5
ββγ-Trimethylbutane	300·6	+ 0·8	301·4	301·4	±0·0
Octane	349·2	+ 1·2	350·4	350·3, 351·0	+0·1
β-Methylheptane	347·0	+ 1·2	348·2	348·7	+0·1
Di*iso*butyl	344·8	+ 1·1	345·9	345·0, 345·5	−0·2
Decane	428·8	+ 1·8	430·6	429·7	−0·2
Di*iso*amyl	424·4	+ 1·8	426·2	422·7, 425·7, 426·9, 427·8	−0·1
Hexacosane	1065·6	+11·6	1077	1082	+0·5
Dotriacontane	1304·4	+17·5	1322	1322	±0·0
Hexacontane	2418·8	+61·2	2480	2480	±0·0
Ethylene	99·4	+ 0·1	99·5	99·5	±0·0
Propylene	139·2	+ 0·2	139·4	139·7	+0·2
Amylene	218·8	+ 0·4	219·2	218·2	−0·5
β-*iso*Amylene	216·6	+ 0·4	217·0	216·9	−0·0
Diallyl	247·6	+ 0·6	248·2	248·2	±0·0

Conversion Table.

Normal paraffins, C_nH_{2n+2}: S.V. $= 2c + (n-2)k$, where $c = 55{\cdot}2$ and $k = 39{\cdot}8$; $[P] =$ S.V. $\times f^n$, where $f = 1{\cdot}0004165$; E.C. = difference between S.V. and $[P]$.

n.	S.V.	[*P*].	E.C.	*n*.	S.V.	[*P*].	E.C.	*n*.	S.V.	[*P*].	E.C.
				21	866·60	874·21	7·61	41	1662·6	1691·2	28·6
2	110·40	110·49	0·09	22	906·40	914·74	8·34	42	1702·4	1732·4	30·0
3	150·20	150·39	0·19	23	946·20	955·31	9·11	43	1742·2	1773·7	31·5
4	190·00	190·32	0·32	24	986·00	995·90	9·90	44	1782·0	1815·0	33·0
5	229·80	230·28	0·48	25	1025·8	1036·5	10·7	45	1821·8	1856·3	34·5
6	269·60	270·27	0·67	26	1065·6	1077·2	11·6	46	1861·6	1897·6	36·0
7	309·40	310·30	0·90	27	1105·4	1117·9	12·5	47	1901·4	1939·0	37·6
8	349·20	350·37	1·17	28	1145·2	1158·6	13·4	48	1941·2	1980·4	39·2
9	389·00	390·46	1·46	29	1185·0	1199·4	14·4	49	1981·0	2021·8	40·8
10	428·80	430·59	1·79	30	1224·8	1240·2	15·4	50	2020·8	2063·3	42·5
11	468·60	470·75+	2·15+	31	1264·6	1281·0	16·4	51	2060·6	2104·8	44·2
12	508·40	510·95−	2·55−	32	1304·4	1321·9	17·5	52	2100·4	2146·4	46·0
13	548·20	551·18	2·98	33	1344·2	1362·8	18·6	53	2140·2	2188·0	47·8
14	588·00	591·44	3·44	34	1384·0	1403·7	19·7	54	2180·0	2229·6	49·6
15	627·80	631·73	3·93	35	1423·8	1444·7	20·9	55	2219·8	2271·2	51·4
16	667·60	672·06	4·46	36	1463·6	1485·7	22·1	56	2259·6	2312·9	53·3
17	707·40	712·43	5·03	37	1503·4	1526·7	23·3	57	2299·4	2354·6	55·2
18	747·20	752·82	5·62	38	1543·2	1567·8	24·6	58	2339·2	2396·4	57·2
19	787·00	793·45+	6·25+	39	1583·0	1608·9	25·9	59	2379·0	2438·2	59·2
20	826·80	833·72	6·92	40	1622·8	1650·1	27·3	60	2418·8	2480·0	61·2

Part II.

Reductions in parachor produced by bent chains of atoms occurring in aliphatic hydrocarbons, alkyl ethers and esters are discussed, and the problem of apportioning suitable values to groups involving linkage of heterogeneous atoms is considered in relation to the parachors of alkyl ethers and esters. In compounds containing a carbonyl group further definite reductions in parachor are found, which appear to be brought about by interaction between the atoms of this group and of neighbouring groups, and the effects are attributed to the polarity of the molecules of these compounds. Among triacyl esters of glycerol and alkyl malonates, and also among alkyl carbonates from propyl onwards, additional interference appears to occur, causing diminution of parachor value to an extent that points to the existence of closely-packed parallel chains of carbon atoms in the molecules.

Reductions in Parachor produced by Bent Chains.—In Part I it was estimated that, on the scale on which the parachor standard value (S.V.) for the group CH_3- is 55·2, the ideal S.V. of a $-CH_2-$ group should be 42·0. When the latter group is attached to two other alkyl groups, however, its effective contribution becomes 39·8, *i.e.*, the grouping (V) (p. 300) involves a diminution in parachor value of 2·2. The whole of this reduction has been assumed to be due to the mutual interference of the two carbon atoms linked to a common carbon atom, the hydrogen atoms being supposed to be too small to produce an appreciable effect. From the parachors for the methyl and ethyl esters of the fatty acids, formic to valeric (see table, p. 307), it appears that S.V., (C)·CH_2·(O), is 39·4, *i.e.*, $C\left\langle \begin{matrix} C \\ O \end{matrix} \right\} = -2{\cdot}6$

To this interference among the atoms in the chains of the molecules of all except the first one or two members of homologous series must be attributed the apparently " singular properties of the methyl group " referred to by Lewis (J., 1940, 36).

The apportioning of a parachor value to a group which involves linkage of heterogeneous atoms cannot be effected by using available data. In, *e.g.*, dimethyl ether, the ideal volume contributions of the methyl groups will not be the same as in propane, in which they are united to an atom of larger size, nor will the interference effect between the two groups be identical in the different molecules since they are not the same distance apart in each. For purposes of calculation it will be satisfactory to allot to CH_3–(O) the same value as for CH_3–(C) and then to obtain a value for (C)·O·(C) by difference.

The parachor of diethyl ether may be taken as 211·1, the mean of the values recorded in " A List of Parachors " (see p. 301); whence

[*P*], $CH_3{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_3$	211·1
Expansion correction (see Part I)	− 0·4
S.V., $CH_3{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_3$	210·7
Deduct 2(C)·CH_2·(O) at 39·4	− 78·8
S.V., $CH_3{\cdot}O{\cdot}CH_3$	131·9
Deduct $2CH_3$– at 55·2	−110·4
S.V., (C)·O·(C)	21·5

A value so obtained, however, is quite arbitrary and is not strictly comparable with group contributions already determined.

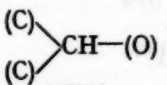
For later use it is necessary to evaluate the groups (VIII) and (IX). The interference corrections in the former are those for $2C<^{C}_{O}$ and $C<^{C}_{C}$, *i.e.*, $-(2 \times 2{\cdot}6 + 2{\cdot}2) = -7{\cdot}4$, and since the ideal value for the group is 28·8 (see Part I), S.V. for (VIII) = ***21·4***; similarly, S.V. for (IX) = $15{\cdot}6 - (3 \times 2{\cdot}6 + 3 \times 2{\cdot}2) =$ ***1·2***.

Using standard values for (C)·O·(C), 21·5, and (C)·CH_2·(O), 39·4, together with those for alkyl groups (obtained in Part I and listed on p. 303), one can compare the calculated and observed parachors of alkyl ethers:

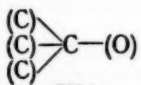
Ethers, $C_nH_{2n+1}{\cdot}O{\cdot}C_mH_{2m+1}$.

Ether.	S.V., calc.	E.C.	[*P*], calc.	[*P*], obs.	Diff., %.
Diethyl	210·7	+0·4	211·1	211·1	±0·0
Ethyl propyl	250·5	+0·6	251·1	252·0	+0·4
Dipropyl	290·3	+0·8	291·1	290·9	−0·1
Dibutyl	369·9	+1·3	371·2	369·9	−0·4
Diamyl	449·5	+1·9	451·4	449·9	−0·3
Diisoamyl	445·1	+1·9	447·0	445·7	−0·3

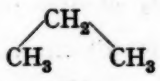
(Each of these parachors is the result of a single determination, except that the value for diethyl ether is the mean of four.)



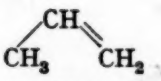
(VIII.)



(IX.)



(X.)



(XI.)

The molecules of paraffins and olefins give little or no evidence of polarity. Consequently, once one has arrived at the bent carbon-chain structure, as in (X) and (XI), no further alteration in the type of structure is to be anticipated as one continues to ascend a series, and molecular volumes, as measured by the parachor, as well as many other physical constants, are found to change with perfect regularity from member to member (although, see p. 300, the CH_2 parachor increments increase as the parachor increases). Also, from the fact that a mean CH_2 S.V. increment of about 39·8 is found in all series of carboxy-esters (formates, acetates, etc.) from the ethyl ester onwards, and from examination of the parachors of alkyl ethers recorded above, it appears that the introduction of an oxygen atom into a carbon chain does not appreciably affect the normal course taken by that chain. With compounds containing a group of marked polarity, such as Cl–(C), Br–(C), I–(C), R·CO·(C), C_6H_5·(C), however, this regularity in the CH_2 increment is only attained after the first few (generally five) members in a series.

Corrections for Compounds containing a Carbonyl Group.—In order to bring his calculated values for the parachors of carboxy-esters into reasonable agreement with the observed values, Sugden (" The Parachor and Valency," 1929, 42) applied an *ad hoc* correction of − 3·2. By employing group values instead of atomic and structural equivalents, one obtains diminutions in parachor value in *all* classes of compounds which contain the

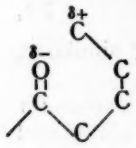
carbonyl group—aldehydes, ketones, and carboxy-acids, as well as their anhydrides and esters. Using standard values (S.V.) for the groups, one discovers that, among the lower members of any one such series, Δ_{CH_2} (the difference in S.V. due to a change in constitution by $-CH_2-$) is less than 39·8, the constant value found among paraffins and olefins. For instance:

Carbonyl Compounds, $C_nH_{2n+1}\cdot CO\cdot R$.

Δ_{CH_2} between S.V. of adjacent members in a series:

Change in group C_nH_{2n+1}·	Δ.	Change in group C_nH_{2n+1}·	Δ.
H– to CH_3–	38·8	C_3H_7– to C_4H_9–	38·1
CH_3– ,, C_2H_5–	37·8	C_4H_9– ,, C_5H_{11}– and onwards ...	39·8 (normal Δ)
C_2H_5– ,, C_3H_7–	39·0		

The reductions in normal value extend as far as the sixth atom in the chain, the oxygen atom being counted as the first. For ketones the reductions apply to both the carbon chains attached to the carbonyl group. No extra reductions are produced by further extension, or by branching, of the carbon chain. It would appear that these contractions in volume are due to the proximity of the doubly-linked oxygen atom to the carbon atoms referred to above, and that therefore there is a bending back of the carbon chain towards the oxygen atom, so as to form a partly-closed ring, the change from the normal direction being presumably a consequence of the polarity of the molecule; the effect ceases just at the point where this imagined ring would be potentially completed (see inset).



With the method of calculation described above (for dimethyl ether), the value to be obtained for the carboxy-group, (C)·CO·O·(C), may be based upon the parachors recorded for ethyl acetate, *viz.*, 215·6, 215·7, 216·9, 217·1, 217·9; mean 216·6.

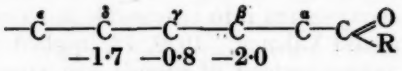
[*P*], $CH_3\cdot CO\cdot O\cdot CH_2\cdot CH_3$	216·6
E.C.	− 0·4
S.V., $CH_3\cdot CO\cdot O\cdot CH_2\cdot CH_3$	216·2
Deduct (C)·CH_2·(O) at 39·4	− 39·4
S.V., $CH_3\cdot CO\cdot O\cdot CH_3$	176·8
Deduct $2CH_3$– at 55·2	−110·4
S.V., (C)·CO·O·(C)	66·4

It is useful also to have a group value for H·CO·O·(C):

S.V., $CH_3\cdot CO\cdot O\cdot CH_3$	176·8
$\Delta CH_3\cdot CO\cdot R/H\cdot CO\cdot R$	− 38·8
S.V., $H\cdot CO\cdot O\cdot CH_3$	138·0
Deduct CH_3– at 55·2	− 55·2
S.V., H·CO·O·(C)	82·8

It must be emphasised again that the values of such groups, which involve linkage of carbon and oxygen, are recorded only for purposes of calculation and are not to be regarded as expressing the volume contributions of these groups on any scale previously employed.

In performing calculations on carbonyl compounds one may give the alkyl groups in the carbon chain attached directly to carbonyl their normal effective values and then apply the necessary " carbonyl corrections ":



Total: −4·5

The correction for the β, γ, or δ carbon atom in the chain is the difference between the Δ value recorded in the table above and the normal Δ (39·8). As pointed out before, in the case of alkyl groups containing branched carbon chains, the carbonyl corrections are found to apply to only one branch of the chain.

The following table contains all the alkyl esters of fatty acids for which parachors are given in the list mentioned on p. 301.

Esters of Fatty Acids, $C_nH_{2n+1}\cdot CO\cdot O\cdot C_mH_{2m+1}$.

Ester.	S.V., calc.	E.C.	[P], calc.	[P], obs. (mean).*	Diff., %.	Corrections applied.
Methyl formate	138·0	+0·1	138·1	138·15 [2]	+0·0	—
Methyl acetate	176·8	+0·3	177·1	176·95 [2]	−0·1	—
Ethyl formate	177·4	+0·3	177·7	177·7 [2]	±0·0	—
Methyl propionate	214·6	+0·4	215·0	215·0 [2]	±0·0	−2·0 : β
Ethyl acetate	216·2	+0·4	216·6	216·6 [5]	±0·0	—
Propyl formate	217·2	+0·4	217·6	216·1	−0·7	—
Methyl butyrate	253·6	+0·6	254·2	254·2 [2]	±0·0	−2·8 : β, γ
Ethyl propionate	254·0	+0·6	254·6	254·5 [3]	−0·0	−2·0 : β
*iso*Butyl formate	254·8	+0·6	255·4	262·4	+2·7	—
Propyl acetate	256·0	+0·6	256·6	256·05 [2]	−0·2	—
Ethyl *iso*butyrate	291·6	+0·8	292·4	292·9	+0·2	−2·0 : β
Methyl valerate	291·7	+0·8	292·5	292·5	±0·0	−4·5 : β, γ, δ
Ethyl butyrate	293·0	+0·8	293·8	293·7 [3]	−0·0	−2·8 : β, γ
*iso*Butyl acetate	293·6	+0·8	294·4	295·1	+0·2	—
Propyl propionate	293·8	+0·8	294·6	295·3	+0·2	−2·0 : β
*iso*Amyl formate	294·6	+0·8	295·4	293·65 [2]	−0·6	—
Ethyl *iso*valerate	330·6	+1·0	331·6	331·9	+0·1	−2·8 : β, γ
Ethyl valerate	331·1	+1·0	332·1	332·1	±0·0	−4·5 : β, γ, δ
*iso*Butyl propionate	331·4	+1·0	332·4	331·8	−0·2	−2·0 : β
Propyl *iso*butyrate	331·4	+1·0	332·4	332·6	+0·1	−2·0 : β
Propyl butyrate	332·8	+1·0	333·8	333·8	±0·0	−2·8 : β, γ
*iso*Amyl acetate	333·4	+1·0	334·4	334·35 [2]	−0·0	—
*iso*Butyl *iso*butyrate	369·0	+1·3	370·3	371·8	+0·4	−2·0 : β
*iso*Butyl butyrate	370·4	+1·3	371·7	370·5	−0·3	−2·8 : β, γ
Propyl valerate	370·9	+1·3	372·2	371·9	−0·1	−4·5 : β, γ, δ
*iso*Amyl propionate	371·2	+1·3	372·5	372·1	−0·1	−2·0 : β
*iso*Amyl butyrate	410·2	+1·6	411·8	409·7 [2]	−0·5	−2·8 : β, γ
Ethyl heptoate	410·7	+1·6	412·3	413·3	+0·2	−4·5 : β, γ, δ
Ethyl octoate	450·5	+2·0	452·5	452·7	+0·0	−4·5 : β, γ, δ
Ethyl pelargonate	490·3	+2·4	492·7	493·6	+0·2	−4·5 : β, γ, δ
*iso*Amyl stearate	965·7	+9·5	975·2	974·2	−0·1	−4·5 : β, γ, δ

* The numbers in brackets show the numbers of determinations upon which the means are based.

The standard values for the carbonyl group, as contained in ketones, and for the aldehyde group may be derived satisfactorily from the mean of the six independent determinations of the parachor of acetone, *viz.*, 160·9, 161·5, 161·5, 161·6, 161·7, 162·0, with the results: S.V. (C)·CO·(C) = *50·9*; S.V. (C)—CHO = *67·3*.

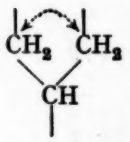
Aldehydes and Ketones, $C_nH_{2n+1}\cdot CO\cdot C_mH_{2m+1}$.

Compound.	S.V., calc.	E.C.	[P], calc.	[P], obs. (mean).	Diff., %.	Corrections applied.
Acetone	161·3	+0·2	161·5	161·5 [6]	±0·0	—
Methyl ethyl ketone	199·1	+0·3	199·4	198·8 [3]	−0·3	−2·0 : β
*iso*Valeraldehyde	236·9	+0·5	237·4	237·5	+0·0	−4·5 : β, γ, δ
Diethyl ketone	236·9	+0·5	237·4	236·8 [2]	−0·3	−4·0 : 2β
Methyl propyl ketone	238·1	+0·5	238·6	238·0 [2]	−0·3	−2·8 : β, γ
Pinacolin	272·1	+0·7	272·8	273·4	+0·2	−2·0 : β
Methyl *iso*butyl ketone	275·7	+0·7	276·4	276·5	+0·0	−2·8 : β, γ
Ethyl propyl ketone	275·9	+0·7	276·6	277·3	+0·2	−4·8 : 2β, γ
Methyl butyl ketone	276·2	+0·7	276·9	276·6 [2]	−0·1	−4·5 : β, γ, δ
Dipropyl ketone	314·9	+0·9	315·8	314·6 [2]	−0·4	−5·6 : 2β, 2γ
Methyl amyl ketone	316·0	+0·9	316·9	319·1	+0·7	−4·5 : β, γ, δ
Heptaldehyde	317·0	+1·0	318·0	318·0	±0·0	−4·5 : β, γ, δ
Methyl hexyl ketone	355·8	+1·2	357·0	356·1 [3]	−0·3	−4·5 : β, γ, δ
Di*iso*butyl ketone	390·1	+1·5	391·6	391·6	±0·0	−5·6 : 2β, 2γ
Methyl heptyl ketone	395·6	+1·5	397·1	396·8	−0·1	−4·5 : β, γ, δ

The above table includes determinations by Cowan, Jeffery, and Vogel (J., 1940, 171), who record parachors for 11 ketones, 7 of which have been previously investigated: in

only one case is their result further from the calculated value than that of any earlier observer; for 5 of the 11 ketones their results are within 0·1% of the calculated parachor, and in 3 more cases within 0·2%.

Interference from Parallel Chains.—The parachors recorded for alternate members of the series of glycerol esters, tricaprin to tristearin, are considerably (some 1·6%) smaller than the calculated values. Examination of the individual differences between observed S.V. and those calculated by using the group values and carbonyl corrections given before shows that these differences can all be represented as $-2{\cdot}2(n+2)$, *i.e.*, the deficit in the S.V. expected amounts to 2·2 units per carbon atom in any one of the three acyl chains. Thus the reduction per trio of carbon atoms in these chains is the same as that produced by the mutual interference of the two outer carbon atoms attached to the central carbon atom in the glycerol nucleus (see inset). This must mean that the two outer chains do not splay, but continue along parallel paths, so that any two corresponding carbon atoms in these chains will be at such a distance from each other as to produce the interference measured by 2·2 parachor units. The molecules will then have a tuning-fork-like configuration, as has indeed been suggested by other physical evidence, *e.g.*, that adduced by Clarkson and Malkin (J., 1934, 666):



$$CH_3{\cdot}[CH_2]_n{\cdot}CO{\cdot}O{\cdot}CH\begin{matrix}<\\ \end{matrix}\begin{matrix}CH_2{\cdot}O{\cdot}CO{\cdot}[CH_2]_n{\cdot}CH_3\\ CH_2{\cdot}O{\cdot}CO{\cdot}[CH_2]_n{\cdot}CH_3\end{matrix}$$

It must be noted, however, that the prongs and stem of the fork are not in the same plane and that each develops a coil in the portion of the chain near the crotch. Calculations based on these assumptions give the following values.

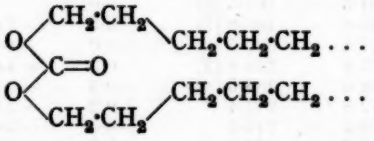
Ester.	S.V., calc. normally.	Extra corrn.: $-2{\cdot}2(n+2)$.	Resultant S.V.	E.C.	[*P*], calc.	[*P*], obs.	Diff., %.
Tricaprin	1406·7	−22·0	1384·7	+19·7	1404	1404	±0·0
Trilaurin	1645·5	−26·4	1619·1	+27·2	1646	1648	+0·1
Trimyristin	1884·3	−30·8	1853·5	+35·7	1889	1892	+0·2
Tripalmitin	2123·1	−35·2	2087·9	+45·4	2133	2127 *	−0·3
Tristearin	2361·9	−39·6	2322·3	+56·4	2379	2378 †	−0·0

* Mean of 2120 and 2134. † Mean of 2376 and 2380.

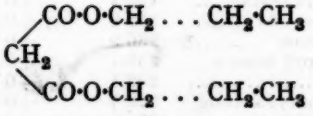
As pointed out in Part I, provided that one accepts the ideas put forward regarding the structure of these compounds, the above results afford very strong evidence for the existence of the " expansion effect " in the parachor, since the theoretical parachors were calculated by using group values and interference corrections derived from the experimental parachors of simple compounds of quite low molecular weight.

Moreover, other series in which similar reductions in parachor are susceptible of similar explanation are those of the alkyl carbonates and malonates, in which, of course, there are two alkyl chains. Among the former, the difference between the mean standard values of the methyl and ethyl esters is 79·0, or almost exactly $2 \times 39{\cdot}4$; but thereafter the mean difference for successive numbers in the series is 77·4 instead of 79·6 [twice the normal (C)·CH_2·(C) value], *i.e.*, there is a reduction of 2·2 for each pair of corresponding carbon

(XII.)



(XIII.)



atoms in the alkyl chains, starting with the third pair. Thus, close packing of the two chains must begin after the second number of the series, as in (XII). This type of structure is in agreement with Thomson's conclusions (J., 1939, 1118) from dipole-moment measurement of the methyl and ethyl esters.

All the parachors except two were determined by Bowden and Butler (*ibid.*, p. 75). Omitting from consideration the parachor they give for the butyl ester,† one finds that S.V. $\begin{matrix}(C){\cdot}O\\ (C){\cdot}O\end{matrix}\!>\!C{=}O$ is *85·5*.

Alkyl Carbonates, R_2CO_3.

R.	Σ group values.	Corrn.	S.V., calc.	E.C.	[*P*], calc.	[*P*], obs.	Diff., %.
CH_3	195·9	0	195·9	+0·3	196·2	196·2	±0·0
C_2H_5	274·7	0	274·7	+0·7	275·4	275·6 *	+0·1
C_3H_7	354·3	−2·2	352·1	+1·2	353·3	352·3	−0·3
C_4H_9	433·9	−4·4	429·5	+1·8	431·3	423·4 †	−1·8
iso-C_4H_9	429·5	−4·4	425·1	+1·8	426·9	428·1	+0·3
C_5H_{11}	513·5	−6·6	506·9	+2·5	509·4	508·2	−0·2
iso-C_5H_{11}	509·1	−6·6	502·5	+2·5	505·0	505·0	±0·0
C_6H_{13}	593·1	−8·8	584·3	+3·4	587·7	587·8	+0·0

* Mean of three values.

† Comparison of the physical constants recorded for the members of the series suggests that the specimen of *n*-butyl carbonate used was not pure.

Assuming that the alkyl chains in malonic esters also are closely packed, one arrives at the general structure (XIII), in which the interference between each pair of corresponding carbon atoms gives rise to a parachor correction of − 2·2 units.

Alkyl Malonates, $CH_2(CO{\cdot}OR)_2$.

R.	Σ group values.	Corrn.	S.V., calc.	E.C.	[*P*], calc.	[*P*], obs.*	Diff., %.
CH_3	283·0	− 2·2	280·8	+0·7	281·5	282·5	+0·3
C_2H_5	361·8	− 4·4	357·4	+1·2	358·6	360·4	+0·5
C_3H_7	441·4	− 6·6	434·8	+1·8	436·6	438·2	+0·4
isoC_3H_7	437·0	− 6·6	430·4	+1·8	432·2	437·1	+1·1
C_4H_9	521·0	− 8·8	512·2	+2·6	514·8	513·8	−0·2
isoC_4H_9	516·6	− 8·8	507·8	+2·5	510·3	511·8	+0·3
isoC_5H_{11}	596·2	−11·0	585·2	+3·4	588·6	586·9	−0·3
C_8H_{17}	839·4	−17·6	821·8	+6·8	828·6	828·7	+0·0

* Beck, Macbeth, and Pennycuick (J., 1932, 2258). Other determinations are: CH_3– 283·1; C_2H_5– 360·3, 362·0 (see list mentioned on p. 301).

Of the 145 parachors so far recorded in this paper (for 96 different compounds—aliphatic hydrocarbons, ethers, carboxy-esters, aldehydes, and ketones), 84 are within 0·2% of the calculated values and another 41 are within 0·5%. Four results which are included differ by more than 1% and are probably unreliable: *iso*butyl formate (+ 2·7%), butyl carbonate (− 1·8%), *iso*propyl malonate (+ 1·1%), and one of the values for hexane (+ 1·1%). The average difference is under 0·3%, and this is reduced to 0·2% if the 96 mean values are considered.

The standard group values derived from the parachors of substances considered in Part II are as follows:

(C)·O·(C), 21·5; (C)·CH_2·(O), 39·4; $\begin{matrix}(C)\\(C)\end{matrix}\!\!>\!CH{\cdot}(O)$, 21·4; $\begin{matrix}(C)\\(C)\\(C)\end{matrix}\!\!>\!C{-}(O)$, 1·2; H·CO·(C), 67·3;

(C)·CO·(C), 50·9; H·CO·O·(C), 82·8; (C)·CO·O·(C), 66·4; $\begin{matrix}(C){\cdot}O\\(C){\cdot}O\end{matrix}\!\!>\!CO$, 85·5.

The following interference correction is involved: $C\!<\!\begin{matrix}C\\O\end{matrix}\}$ − 2·6; and corrections for β, γ, and δ C atoms in alkyl chains attached to $>C{=}O$: β − 2·0, γ − 0·8, δ − 1·7.

The author thanks Dr. J. Colvin, University of Leeds, and Dr. K. G. Denbigh, University College, Southampton, for the interest they have taken in his work, and for valuable suggestions and advice given during the preparation of this paper.

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57.—*Benzanthrones. Part IV. The Synthesis of 2- and 4-Methyl-1-phenylnaphthalene-2′-carboxylic Acids. The Conversion of Benzfluorenones into Benzanthrones.*

By Fawzy Ghali Baddar.

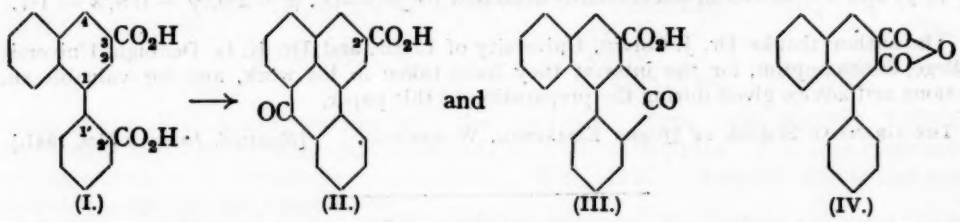
Interaction between diazotised methyl anthranilate and 1- and 2-methylnaphthalene gave a mixture of acids and 1-phenyl-2-methylnaphthalene-2′-carboxylic acid respectively.

Cyclisation of *o*-α-naphthylbenzoic acid, and of *1-phenyl-4-methylnaphthalene-2′-carboxylic acid*, gave a mixture of a benzfluorenone and a benzanthrone. Contrary to Schaarschmidt the ring closure of 1-phenylnaphthalene-2′ : 3-dicarboxylic acid led to the formation of a trace of 3 : 4-benzfluorenone-1-carboxylic acid besides the main product, *meso*benzanthrone-2′-carboxylic acid. The latter compound was also obtained by heating 1-phenylnaphthalene-2 : 3-dicarboxylic anhydride with aluminium chloride and sodium chloride. Similar treatment of 3 : 4-benzfluorenone with aluminium chloride gave *meso*benzanthrone.

1-Phenyl-2-methylnaphthalene-2′-carboxylic acid was prepared by the condensation of diazotised methyl anthranilate with 2-methylnaphthalene at 45° (cf. Grieve and Hey, J., 1938, 108; Heilbron, Hey, and Wilkinson, *ibid.*, p. 699). *1-Phenyl-4-methylnaphthalene-2′-carboxylic acid*, which could not be obtained from 1-methylnaphthalene by this method, was easily prepared from *1-iodo-4-methylnaphthalene* and methyl *o*-iodobenzoate by the Ullmann reaction (cf. Baddar and Warren, Part I, J., 1938, 401).

In Part I (*loc. cit.*) it was stated that, contrary to Schaarschmidt and Georgeacopol (*Ber.*, 1918, **51**, 1082), *o*-α-naphthylbenzoic acid and its 4-ethyl derivative gave on ring closure, both with phosphorus pentachloride, followed by aluminium chloride, and with sulphuric acid, a mixture of a benzfluorenone and a benzanthrone. Grieve and Hey (*loc. cit.*) reported the same results as Schaarschmidt and Georgeacopol (*loc. cit.*), without the isolation of 3 : 4-benzfluorenone. The present author has confirmed the results of Baddar and Warren: the cyclisation of *o*-α-naphthylbenzoic acid with phosphorus pentachloride, followed by aluminium chloride, at 20° or at 60° and with concentrated sulphuric acid at 0°, 20°, or 50° gave a mixture of benzfluorenone and benzanthrone. The same results were obtained when 10% boric acid–sulphuric acid solution or phosphoric oxide was used. Cyclisation of 1-phenyl-4-methylnaphthalene-2′-carboxylic acid by aluminium chloride or sulphuric acid gave a mixture of *2-methyl-3 : 4-benzfluorenone* and 1′-methyl-*meso*benzanthrone, whereas ring closure of 1-phenyl-2-methylnaphthalene-2′-carboxylic acid gives (Baddar and Warren, Part II, J., 1939, 944) only 3′-methyl*meso*benzanthrone owing to the blocking of the 2-position.

Schaarschmidt (*Ber.*, 1917, **50**, 294) isolated only *meso*benzanthrone-2′-carboxylic acid (II) by the ring closure of 1-phenylnaphthalene-2′ : 3-dicarboxylic acid (I) with aluminium chloride or concentrated sulphuric acid: the present author isolated the same product (II) and inferred the formation also of a trace of 3 : 4-benzfluorenone-1-carboxylic acid (III) from the production of 3 : 4-benzfluorenone on decarboxylation.



(I.) (II.) (III.) (IV.)

The inference that only a trace of 3 : 4-benzfluorenone-1-carboxylic acid (III) is formed suggests that the reactivity of the carbon atom in position 2 is diminished by the proximity of the carboxyl group. Such a deactivating effect appears to be responsible for the production of 1-phenylnaphthalene-2′ : 3-dicarboxylic acid (I), by the fusion of 3 : 4-

benzfluorenone-1-carboxylic acid (III) with potash (Schaarschmidt, *loc. cit.*), and not a mixture of two acids as in the case of benzfluorenone itself (Schaarschmidt and Georgeacopol, *loc. cit.*).

Stobbe (*Ber.*, 1907, **40**, 3383) stated that when 1-phenylnaphthalene-2 : 3-dicarboxylic anhydride (IV) was treated with cold concentrated sulphuric acid, 3 : 4-benzfluorenone-1-carboxylic acid (III) was obtained. Schaarschmidt and Korten (*Ber.*, 1918, **51**, 1074), on trying to hasten this reaction by using hot 91% sulphuric acid, obtained *meso*benzanthrone-2′-carboxylic acid (II) in poor yield. The latter authors stated also that, although benzfluorenone was sulphonated on similar treatment, yet the development of fluorescence could be considered as an indication of its partial transformation into *meso*benzanthrone.

The best reagent for converting a benzfluorenone into a benzanthrone is a melt of aluminium chloride and sodium chloride. The old method of Schaarschmidt (*loc. cit.*) for converting (IV) quantitatively into (II) was carried out in three steps. It is possible, however, under the influence of aluminium chloride to effect a direct conversion in good yield. The transformation undoubtedly includes the formation of 3 : 4-benzfluorenone-1-carboxylic acid (III) as an intermediate product, which is then converted into *meso*benzanthrone-2′-carboxylic acid (II). The mechanism of the reaction is not known, but it involves the fission of the five-membered ring, followed by formation of the six-membered one.

Experimental.

1-Phenyl-2-methylnaphthalene-2′-carboxylic Acid.—A mixture of diazotised methyl anthranilate (25 g.; 1 mol.) and 2-methylnaphthalene (50 g.; 2·1 mols.) in 200 c.c. of carbon tetrachloride was stirred at 0—5° while sodium hydroxide solution (31·5 g., 2 mols., in 50 c.c. of water) was added during 1 hour. The temperature was kept at 0—10° for 1½ hours, raised to 45° during 3½ hours, and maintained for 5 hours. The carbon tetrachloride layer was separated, washed with sodium hydroxide solution and with water, and distilled at the ordinary pressure to remove unchanged 2-methylnaphthalene and the by-products, b. p. 230—250°; the remainder was distilled under reduced pressure, and the fraction, b. p. 195—215°/7 mm., hydrolysed. The acid obtained was twice crystallised from methyl alcohol to give 1-phenyl-2-methylnaphthalene-2′-carboxylic acid (1·1 g.), m. p. 188° (Found: C, 82·3; H, 5·3. Calc. for $C_{18}H_{14}O_2$: C, 82·4; H, 5·4%).

1-Iodo-4-methylnaphthalene was obtained from 4-methyl-α-naphthylamine as an orange-yellow mobile liquid, b. p. 159°/6 mm., in 51% yield (Found: I, 47·3. $C_{11}H_9I$ requires I, 47·4%).

1-Iodo-4-methylnaphthalene (3·8 g.; 1 mol.), methyl *o*-iodobenzoate (8 g.; 2·1 mols.), and copper bronze (4 g.; 4·5 mols.) were heated at 180—190° for 5 hours. The resulting *1-phenyl-4-methylnaphthalene-2′-carboxylic acid* crystallised from methyl alcohol in colourless rods (0·6 g.), m. p. 200—201° (Found: C, 82·4; H, 5·4. $C_{18}H_{14}O_2$ requires C, 82·4; H, 5·4%). The yield of diphenic acid was 2·1 g. (for details, see Part I, *loc. cit.*).

Ring closure of the acid chloride of the above acid with aluminium chloride, and fractional crystallisation of the product from methyl alcohol and then from acetic acid, gave *2-methyl-3 : 4-benzfluorenone* in orange-red crystals, m. p. 148—149° (Found: C, 88·6; H, 5·3. $C_{18}H_{12}O$ requires C, 88·5; H, 5·0%), and 1′-methyl*meso*benzanthrone in yellow silky needles, m. p. 162—163° (F.P. 631,995; *Centr.*, 1928, I, 2210, gives m. p. 164°) (Found: C, 88·3; H, 5·0. Calc. for $C_{18}H_{12}O$: C, 88·5; H, 5·0%).

Ring closure of the acid with 90% sulphuric acid resulted mainly in the benzfluorenone. The isolation of pure 1′-methyl*meso*benzanthrone, which was rather tedious by the ordinary method of fractional crystallisation, was easily accomplished by heating the mixture with concentrated sulphuric acid at 100° for 2 hours, whereby the benzfluorenone was sulphonated.

meso*Benzanthrone-2′-carboxylic Acid.*—1-Phenylnaphthalene-2 : 3-dicarboxylic anhydride (2 g.) was added to a melt of aluminium chloride (20 g.) and sodium chloride (4 g.) at 100°. The temperature was raised to 150° during ½ hour and kept at 140—150° for 2½ hours. The hot brown mixture was poured on ice and digested with dilute hydrochloric acid. After filtration the product was dissolved in hot sodium carbonate solution, boiled (charcoal), filtered, and acidified with hydrochloric acid. The precipitated jelly-like acid was filtered off, dried, and crystallised from nitrobenzene, from which *meso*benzanthrone-2′-carboxylic acid was obtained in 85% yield in silky yellow needles, m. p. 347—348°, undepressed by an authentic specimen (Schaarschmidt, *loc. cit.*, and Schaarschmidt and Korten, *loc. cit.*, give m. p. 347°).

meso*Benzanthrone*.—The preceding acid (0·35 g.; 1 mol.) and copper-bronze (0·08 g.; 1 mol.) were refluxed in quinoline (5 c.c.) for 1 hour, benzene added, and the filtered solution repeatedly extracted with dilute hydrochloric acid. The product was crystallised from methyl alcohol, giving *meso*benzanthrone in yellow needles, m. p. and mixed m. p. 170°, in nearly quantitative yield.

3 : 4-*Benzfluorenone*.—3 : 4-Benzfluorenone-1-carboxylic acid was treated with copper-bronze as described above. The product was crystallised from alcohol, from which 3 : 4-benzfluorenone separated in orange crystals, m. p. 160°, identical with an authentic specimen. This method gave a better yield (71%) than that of Schaarschmidt and Georgeacopol (*loc. cit.*) and Schaarschmidt (*Ber.*, 1916, **49**, 1540).

Conversion of 3 : 4-*Benzfluorenone into* meso*Benzanthrone*.—Benzfluorenone (1·2 g.) was added to a melt of aluminium chloride and sodium chloride (15 g. and 3 g. respectively) at 100°, and the temperature raised to 145° during ½ hour and maintained for 1½ hours. The product was poured on ice, and the precipitated sticky solid extracted with benzene, decolourised with animal charcoal, and crystallised from methyl alcohol to give *meso*benzanthrone, m. p. 160—165°, in 62% yield. After two crystallisations from alcohol the m. p. was 169—170°, not depressed by an authentic specimen.

Ring Closure of o-α-*Naphthylbenzoic Acid*.—(1) The acid was mixed with concentrated sulphuric acid and left either (*a*) in the ice chest for 3 days or (*b*) at room temperature (20°) for 24 hours. (2) The acid chloride, prepared by means of phosphorus pentachloride, was cooled in ice, treated with aluminium chloride, and left overnight at room temperature. (3) The acid (0·2 g.) was dissolved in benzene (4 c.c.) and treated with phosphoric oxide (2 g.). The mixture was heated for 4 hours at 60° and poured on ice, and the product worked up in the usual way. In all three cases the product was a mixture of benzanthrone and benzfluorenone.

Ring Closure of 1-*Phenylnaphthalene*-2′ : 3-*dicarboxylic Acid*.—The crystallised acid was refluxed for 4 hours with acetic anhydride (5 parts) to convert any trace of the isomeric 1-phenylnaphthalene-2 : 3-dicarboxylic acid into its anhydride (IV). The acetic anhydride solution was decomposed with warm aqueous sodium carbonate, filtered from any insoluble anhydride (IV), and acidified. The precipitated acid was crystallised from acetic acid and cyclised with concentrated sulphuric acid. The product (0·85 g.) was separated into its constituents by two methods: (*a*) Crystallisation from nitrobenzene gave pure *meso*benzanthrone-2′-carboxylic acid. The mother-liquor was steam-distilled; the residue (0·1 g.) gave pure benzfluorenone on decarboxylation. (*b*) The product was decarboxylated; fractional crystallisation from methyl alcohol then gave *meso*benzanthrone and a trace of benzfluorenone.

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58. *Optically Active Tetrahydrofurfuryl Alcohol.*

By MICHAEL P. BALFE, MICHAEL IRWIN, and JOSEPH KENYON.

dl-Tetrahydrofurfuryl alcohol, now commercially available, is easily separated into its optically pure (+)- and (−)-forms. The rotatory dispersion of the optically active alcohol is anomalous and that of a number of its derivatives is complex. The anomalous dispersion is probably caused by anisotropic absorption bands associated with either (or both) of the oxygen atoms in the molecule.

In view of the ease with which the optically active alcohol is obtained, and its interesting optical properties, it may prove a useful material in studies on optical rotatory power.

dl-TETRAHYDROFURFURYL alcohol, b. p. 177—179°, obtained by fractional distillation of the commercial liquid, is converted by the usual method into its ***hydrogen phthalate***, which readily crystallises in 90% yield and is raised to its maximum melting point after one recrystallisation. Some 5% of the ester separates as an oil, which can be separated, *via* the brucine salt, into the same (+)- and (−)-*hydrogen phthalates* as are obtained from the crystalline *dl*-alcohol. It appears, therefore, that part of the *dl*-ester remains oily because it contains impurities; there is no evidence that it contains *cis*- and *trans*-isomerides derived from a hypothetical, but improbable, non-planar configuration of the tetrahydro-

furan nucleus (according to Hibbert and Allen, *J. Amer. Chem. Soc.*, 1932, **54**, 4115, the tetrahydrofuran ring is flat).

By fractional crystallisation of its brucine salt, the *dl*-hydrogen phthalate is readily separated into the (+)- and (−)-forms, the latter being obtained in better yield. From these, the (+)- and the (−)-alcohol are obtained, with no racemisation, by steam-distillation from 5N-aqueous sodium hydroxide. [We define as (+) that alcohol which is dextrorotatory at λ_{5893} and is obtained from the (+)phthalate.] Table I records the observed rotatory powers of the (−)alcohol, determined in the visible and ultra-violet spectra by Dr. C. B. Allsopp (absorption commenced at 3603 A.). Our own observations (observed and specific rotatory powers) on (+)- and (−)-alcohols in the visible spectrum are in Table II. The plot of α against λ from the data in Table I shows that the rotatory

TABLE I.

Observed Rotatory Powers of (−)*Tetrahydrofurfuryl Alcohol* (l = 2·0, t = 20°). (Wavelengths above 4600 were observed visually, those below 4600 photographically. Absorption commenced at λ_{3603}.)

λ.	α.	λ.	α.	λ.	α.	λ.	α.	λ.	α.
6708	−4·701°	5461	−3·954°	4384	+ 4·0°	3878	+14·0°	3603	+33·0°
6438	−4·971	5086	−2·722	4282	+ 6·0	3917	+16·0	3392	+52·0
6104	−4·587	4800	−0·961	4191	+ 8·0	3872	+18·0	3340	+60·0
5893	−4·539	4603	+1·175	4108	+10·0	3767	+23·0		
5780	−4·472	4529	+2·0	4032	+12·0	3669	+28·0		

TABLE II.

Rotatory Powers of (+)- *and* (−)-*Tetrahydrofurfuryl Alcohol.*

	(+)Alcohol.		(−)Alcohol.							
Temp.	20°		18°		20°		41°		59·5°	
	(*l* = 2).		(*l* = 0·5).		(*l* = 2).		(*l* = 0·5).		(*l* = 0·5).	
λ.	α.	[α].	α.	[α].	α.	[α].	α.	[α].	α.	[α].
6438	+4·87°	+2·28°	−1·31°	−2·45°	−4·85°	−2·28°	−1·19°	−2·28°	−1·17°	−2·28°
5893	+4·64	+2·18	−1·18	−2·21	−4·65	−2·18	−1·05	−2·01	−1·03	−2·0
5780	+4·46	+2·10	−1·06	−1·99	−4·44	−2·09	−0·99	−1·89	−1·00	−1·98
5461	+3·98	+1·87	−0·98	−1·84	−3·95	−1·86	−0·89	−1·70	−0·86	−1·67
5086	+2·64	+1·24	−0·64	−1·20	−2·60	−1·22	−0·50	−0·96	−0·46	−0·89
4800	+0·78	+0·37	−0·28	−0·52	—	—	−0·10	−0·19	−0·01	−0·02
4358	−4·63	−2·18	+1·13	+2·12	+4·80	+2·25	+1·31	+2·50	+1·43	+2·78

dispersion is anomalous, since the curve passes through a maximum and a reversal of sign. This is not unexpected, since anisotropic absorption bands due to either oxygen atom may contribute partial rotations to the observed rotatory powers. In support of this may be cited the following cases. In amyl alcohol (2-methyl-1-butanol), as in tetrahydrofurfuryl alcohol, a methylene group is interposed between the hydroxyl group and the asymmetric carbon atom. The high dispersion of amyl alcohol (Lowry, " Optical Rotatory Power," 1935, p. 266) compared with that of the secondary alcohols suggests that its dispersion is not really simple. Similarly, the interposition of a methylene group between the carboxyl group and the asymmetric carbon atom converts the simple dispersion of *iso*-valeric acid and its esters into the complex dispersion of β-methylvaleric acid and its esters (Levene *et al.*, *J. Chem. Physics*, 1933, **1**, 662, 667). With regard to the ethereal oxygen atom, it may be observed that the *n*-alkyl ethers of (+)-γ-nonanol show complex dispersion, whereas dispersion of (+)-γ-nonanol itself is simple (Kenyon and Barnes, J., 1924, **125**, 1395).

When the rotatory powers of (−)tetrahydrofurfuryl alcohol are observed in a series of aqueous solutions of increasing dilution (Tables I and III, the curve for the highest concentration being that of the homogeneous alcohol), the results can be plotted as a family of curves in which the points of inflection, maxima, and changes of sign move progressively towards shorter wave-lengths as the dilution is increased. A similar series of curves is given by aqueous solutions of tartaric acid (Lowry and Austin, *Phil. Trans.*, 1922, *A*, **122**, 249). A somewhat similar series of curves is also given by the rotatory powers of 5%

TABLE III.

Specific Rotatory Powers of (−)Tetrahydrofurfuryl Alcohol in Aqueous Solutions (l = 2·0; t = 17·0°).

λ.	c = 80·0.	70·0.	60·0.	50·0.	40·0.	20·0.	10·0.	5·0.
6438	−3·16°	−4·37°	−5·63°	−7·52°	−8·70°	−11·68°	−12·85°	−14·0°
5893	3·34	4·86	6·37	8·61	10·03	13·57	15·10	16·15
5780	3·36	4·91	6·54	8·90	10·47	14·18	16·75	—
5461	3·30	5·13	6·93	9·62	11·23	15·55	17·15	17·7
5086	2·98	5·19	7·37	10·48	12·35	17·40	19·35	20·6
4800	2·48	5·17	7·49	11·09	13·12	18·85	20·80	22·4
4358	0·65	4·12	7·21	11·25	14·07	20·94	24·85	26·9

solutions of (−)tetrahydrofurfuryl alcohol in the *n*-aliphatic alcohols from methyl to *n*-amyl (Table IV), though the relative positions of the rotatory powers in *n*-propyl and *n*-amyl alcohols are transposed.

TABLE IV.

Specific Rotatory Powers of (−)Tetrahydrofurfuryl Alcohol in Solution in n-*Alcohols* (l = 2·0; t = 20°).

Solvent.	MeOH.	EtOH.	Pr^{n}OH.	Am^{n}OH.	Solvent.	MeOH.	EtOH.	Pr^{n}OH.	Am^{n}OH.
	c = 5·20.	5·06.	4·98.	5·06.		c = 5·20.	5·06.	4·98.	5·06.
λ.					λ.				
6438	− 8·8°	−1·68°	+1·50°	−0·49°	5086	−11·6°	+1·01°	+4·21°	+2·57°
5893	− 9·5	−1·38	+1·80	+0·30	4800	−12·6	—	+5·01	+3·66
5780	− 9·7	—	+2·31	+1·19	4358	−13·1	+5·14	+9·53	+7·12
5461	−10·2	±0	+3·21	+1·58					

A curve of anomalous dispersion, such as is shown by the present alcohol, would be expected to conform to a two-term Drude equation (as Hunter, Thesis, London, 1922, points out, the rotatory powers of organic compounds are not usually of sufficient magnitude to show the effect of a third term). However, we have not been able to derive such an equation to fit the results recorded in Table I.

Table II shows the variation of rotatory dispersion of the (−)alcohol with change of temperature. The variation of the dispersion ratio with temperature is small: it changes only from 1·15 to 1·66 between 18° and 59·5°, and is in contrast to the cases of, *e.g.*, tartaric acid and its esters (for the ethyl ester the dispersion ratio changes from 0·27 to 0·8 between 20° and 64°). This is in agreement with the suggestion that the anomalous dispersion of tetrahydrofurfuryl alcohol is not due to the existence of labile structures such as have been postulated to explain the anomalous dispersion of tartaric acid and its esters, but is a fixed property of the alcohol molecule, *i.e.*, is derived from the two oxygen atoms in the molecule.

Table V records the rotatory powers of the (−)alcohol in a number of other solvents. These, as would be expected, also show evidence of complexity. In two cases reversals

TABLE V.

Specific Rotatory Powers of (−)Tetrahydrofurfuryl Alcohol in Various Solvents (l, 2·0; t, 20°).

Solvent.	6N-HCl.	5N-NaOH.	$MeNO_2$.	$CHCl_3$.	C_5H_5N.	Dioxan.	C_6H_6.	CS_2.	Et_2O.	Pr$^{\beta}$OH.
	c = 5·00.	5·09.	5·14.	5·34.	5·10.	5·22.	5·48.	5·32.	5·60.	5·11.
λ.										
6438	−18·10°	−8·83°	−14·8°	−15·85°	−15·9°	−7·2°	−6·2°	−6·1°	−4·5°	+3·21°
5893	22·3	9·23	17·5	17·1	17·1	7·2	6·1	5·2	3·9	4·55
5780	23·7	—	—	18·0	—	—	—	—	—	4·72
5461	25·7	10·70	19·7	18·9	18·6	7·2	6·1	4·1	3·3	5·74
5086	28·8	—	—	22·5	—	—	—	—	—	8·06
4800	31·3	—	—	23·9	—	—	—	—	—	10·29
4358	38·8	12·80	26·2	27·1	26·7	7·2	2·3	+1·5	+0·9	14·18

of sign occur, and in all cases the dispersion constants $\alpha_{4358}/\alpha_{5461}$ are far removed from the value 1·65 approximately characteristic of the simple dispersion of the *sec.*-carbinols, or the calculated value of 1·57 for simple dispersion. The results in 1 : 4-dioxan solution

are remarkable, the rotatory power in this case being independent of wave-length, in the visible spectrum. Complex dispersion is also shown by a number of derivatives of the alcohol. The hydrogen phthalate in a variety of solvents (Table VI), and the *p*-toluenesulphonate, p-*xenylurethane*, and p-*nitrobenzoate* (Table VII), in respect of dispersion constant and curvature of the plot of $1/\alpha$ against λ^2, are obviously complex. The benzoate and acetate have dispersion constants which could correspond to simple dispersion, and the plots of $1/\alpha$ against λ^2 for these esters can only be represented as straight lines, the divergences being random and probably due to experimental error. We think it likely, however, that this apparent simplicity would not be maintained if the dispersion curve were followed into the ultra-violet spectrum.

TABLE VI.

Specific Rotatory Powers of (−)*Tetrahydrofurfuryl Hydrogen Phthalate in Various Solvents* (l = 2·0; t = 17—20°).

Solvent.	$CHCl_3$.	C_6H_6.	HOAc.	Dioxan.	C_5H_5N.	EtOH.	Et_2O.
	c = 5·04.	5·02.	5·04.	5·44.	5·16.	5·01.	5·28.
λ.							
6438	−25·3°	−20·0°	−16·4°	−10·93°	—	−6·6°	−3·3°
5893	31·8	27·0	20·7	13·14	−10·16°	7·3	4·1
5780	33·4	28·8	21·4	14·24	10·35	7·5	4·5
5461	38·0	31·8	23·7	14·98	10·8	7·9	4·6
5086	43·6	37·5	28·7	18·93	—	9·1	5·7
4800	53·7	53·5	33·3	20·95	—	10·1	6·1
4358	68·0	55·6	42·2	26·47	16·35	11·6	6·3

TABLE VII.

Rotatory Powers of Other Derivatives of (−)*Tetrahydrofurfuryl Alcohol* (t = 20·0°).

Derivative.	*p*-Toluenesulphonate.		*p*-Xenylurethane.	*p*-Nitrobenzoate.	Benzoate.	Acetate.
Solvent.	None.*	CS_2.	$CHCl_3$.	$CHCl_3$.	None.	None.
	c = —	9·13.	4.87.	5·04.	—	—
	l = 0·25.	2·0.	2·0.	2·0.	0·5.	0·5.
λ.						
6438	−12·08°	−1·26°	−21·7°	—	13·0°	−15·3°
5893	13·88	0·93	27·1	−31·6°	15·5	17·9
5780	14·32	0·81	30·0	32·6	16·3	18·8
5461	15·82	0·66	33·5	36·5	18·0	20·8
5086	18·92	0·33	38·4	—	20·8	23·6
4800	21·08	1·48	42·4	—	23·4	26·2
4358	23·28	3·67	—	65·5	28·2	31·1

* This column gives observed rotatory powers; all the other columns give specific rotatory powers.

EXPERIMENTAL.

Commercial tetrahydrofurfuryl alcohol was redistilled, and the fraction of b. p. 177—179°, $n_D^{16°}$ 1·4529, collected. Its phenylurethane has m. p. 62° (Wienhaus, *Ber.*, 1920, **53**, 1656, gives m. p. 61°); its p-*xenylurethane*, short needles, m. p. 104—106° from ether and light petroleum (Found: N, 5·1. $C_{18}H_{19}O_3H$ requires N, 4·7%); and its *p*-toluenesulphonate, m. p. 39—40° (Barger, Robinson, and Smith, J., 1937, 720, give m. p. 38·7—39·1°).

dl-*Tetrahydrofurfuryl Hydrogen Phthalate.*—A mixture of the alcohol (102 g.), phthalic anhydride (148 g.), and pyridine (100 g.) was heated for 2 hours on the steam-bath, and the product worked up in the usual way. The resulting hydrogen phthalic ester was obtained as an oil (233 g.), which after several days set—not quite completely—to a compact mass of irregular rhombs, m. p. 44—46°. From ether–light petroleum it crystallised slowly in hard, glassy rhombs, m. p. 62—64° (Found, by titration with NaOH: *M*, 249. $C_{13}H_{14}O_5$ requires *M*, 250). On saponification it yielded *dl*-tetrahydrofurfuryl alcohol with $n_D^{16°}$ 1·4515.

l-*Tetrahydrofurfuryl Hydrogen Phthalate.*—Brucine (438 g.) was dissolved in a hot solution of the *dl*-ester (278 g.) in acetone (1500 c.c.). The salt which separated on cooling, in rosettes of short needles (about 350 g.), was removed by filtration and decomposed with dilute hydrochloric acid. The liberated l-*ester*, which usually had $[\alpha]_{5893}$ −20° (*ca.*) in chloroform solution,

was recrystallised three or four times from ether–light petroleum until its rotatory power was constant; it formed large glassy rhombs, m. p. 82—83·5° (Found, by titration with NaOH: *M*, 247). Rotatory powers are in Table VI.

This fractional crystallisation of *l* + *dl*-hydrogen phthalic ester is the more efficient method of resolution, for the original brucine salt, after being recrystallised four times from acetone or methyl acetate, yields a hydrogen phthalate of only approximately 92% optical purity.

d-*Tetrahydrofurfuryl Hydrogen Phthalate*.—The more soluble fractions of brucine salt contained in the filtrates yielded on decomposition with hydrochloric acid *d* + *dl*-hydrogen phthalic ester (with $[\alpha]_{5893}$ + 24° in chloroform), from which, after several crystallisations from ether and light petroleum, optically pure d-*tetrahydrofurfuryl hydrogen phthalate* was readily obtained as glassy rhombs, m. p. 82—83·5° (Found, by titration with NaOH: *M*, 252).

When ethereal solutions of equal amounts of the *d*- and the *l*-hydrogen phthalic ester were mixed and allowed to evaporate, glassy rhombs of the *dl*-ester, m. p. 62—64°, separated.

l-Tetrahydrofurfuryl alcohol was obtained in almost theoretical yield when the *l*-hydrogen phthalate was dissolved in sodium hydroxide (5N; 2·2 mols.), and the solution steam-distilled. The aqueous distillate was saturated with potassium carbonate and extracted several times with ether. *l*-Tetrahydrofurfuryl alcohol has b. p. 74·5°/14 mm., $n_{D}^{20°}$ 1·4529; $d_{4°}^{17·5°}$ 1·064, $d_{4°}^{23·5°}$ 1·051, $d_{4°}^{47·5°}$ 1·038, $d_{4°}^{61·5°}$ 1·027. Wienhaus (*loc. cit.*) gives $d_{0°}^{20°}$ 1·054 for the *dl*-alcohol.

Its rotatory powers in the homogeneous state at different temperatures and in various solutions at room temperature are recorded in Tables I—V. A portion was reconverted into its hydrogen phthalate; this had $[\alpha]_{5893}$ −32·8° (*l*, 2; *c*, 5·160 in chloroform), showing that no racemisation occurred during the saponification.

d-Tetrahydrofurfuryl alcohol, obtained in a similar manner from the *d*-hydrogen phthalate, had b. p. 79°/20 mm., $n_{D}^{17·0°}$ 1·4531; its rotatory powers are recorded in Table II.

l-*Tetrahydrofurfuryl* p-*nitrobenzoate* (Table VII), prepared by Einhorn's method, separated from ether and light petroleum in long, slender, flat, almost colourless needles, m. p. 36—37° (Found: N, 5·7. $C_{12}H_{13}O_5N$ requires N, 5·6%). The corresponding *dl*-compound, flat needles, had m. p. 48—49°. The acetate, prepared by Einhorn's method, had b. p. 90°/20 mm., $n_{D}^{20°}$ 1·4371, and the benzoate, b. p. 173°/20 mm., $n_{D}^{19·5°}$ 1·5242. Rotatory powers of both these esters are in Table VII. [For the corresponding *dl*-acetate, Zanetti (*J. Amer. Chem. Soc.*, 1928, **50**, 1821) gives b. p. 194—195°, $d_{0°}^{20°}$ 1·061; and for the *dl*-benzoate b. p. 300—302°, $d_{0°}^{20°}$ 1·137, but he does not give the refractive indices.]

l-Tetrahydrofurfuryl *p*-toluenesulphonate (Table VII) formed massive crystalline plates, m. p. 25°.

dl-Tetrahydrofurfuryl hydrogen phthalate (5 g.) was dissolved in anhydrous formic acid (8 g.) and heated on the steam-bath during several hours, and then left at room temperature for several months, but was recovered completely unchanged. Attempts to prepare the formate by reaction of the alcohol with formic-acetic anhydride were unsuccessful, dark viscous products being formed, possibly by opening of the tetrahydrofuran ring (compare Robinson and Smith, J., 1936, 195).

Thanks are due to Dr. C. B. Allsopp for the determinations recorded in Table I, and to the Government Grants Committee of the Royal Society and Imperial Chemical Industries Ltd. for grants.

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59. *Optically Active αγ-Diethylallyl Alcohol.*

By B. C. PLATT.

αγ-Diethylallyl alcohol has been synthesised and resolved. The properties of the optically active alcohol are compared with those of its lower homologue, αγ-dimethylallyl alcohol.

IN view of the anomalous behaviour of optically active αγ-dimethylallyl alcohol (Hills, Kenyon, and Phillips, J., 1936, 576), it was thought desirable to prepare a second optically active, symmetrically disubstituted αγ-allyl alcohol. The next homologue, *αγ-diethylallyl alcohol*, was accordingly investigated. The *dl*-alcohol, prepared by the usual Grignard

method in good yield, was resolved by fractional crystallisation of the strychnine salt of its *hydrogen phthalic ester*, both *d*- and *l*-forms of the hydrogen phthalic ester being obtained. The identity in magnitude of the rotatory powers of the *d*- and *l*-hydrogen phthalic esters and the inability of crystallisation to raise their rotatory powers may be taken as evidence that the optical resolution was complete. The optically pure alcohol was obtained by hydrolysis of the optically pure hydrogen phthalic ester with either concentrated aqueous sodium hydroxide or alcoholic potassium hydroxide; both these reagents bring about very little racemisation, for the optically active alcohol, so obtained, can be reconverted into its hydrogen phthalic ester with but 10% overall loss of rotatory power.

The (+)-hydrogen phthalic esters of αγ-dimethyl- and αγ-diethyl-allyl alcohols are similar in that their specific rotatory powers are essentially unaffected by change of concentration in solvents *except* in carbon disulphide solution (Table I). In this solvent, however, change of the sign of rotation is effected by alteration in the concentration, but the reason for this effect is not apparent.

TABLE I.

Specific Rotatory Powers of (−)-αγ-*Diethylallyl Hydrogen Phthalate in Various Solvents at Room Temperature* (1, 2).

Solvent.	*c.*	$[\alpha]_{6438}$.	$[\alpha]_{5893}$.	$[\alpha]_{5780}$.	$[\alpha]_{5461}$.	$[\alpha]_{5086}$.	$[\alpha]_{4358}$.
Et_2O	5·0800	−23·8°	−29·5°	−30·0°	−35·7°	−44·1°	−70·9°
,, ...	2·5400	−24·6	−29·5	−33·8	−36·6	−46·2	−73·9
EtOH	4·8320	−25·6	−27·8	−30·6	−34·7	−43·0	−71·1
C_5H_5N	5·1635	−17·4	−20·4	—	−26·9	−32·9	−60·0
C_6H_6	5·0170	−14·8	−20·3	−22·8	−24·3	−30·2	−52·3
,, ...	2·5085	−16·9	−19·5	−22·9	−23·9	−30·9	−54·0
$CHCl_3$	4·4660	—	−15·1	−17·0	−19·6	—	−38·6
,, ...	2·2452	−10·0 *	−16·0 *	−16·9 *	−18·3 *	−25·1 *	−37·9 *
CS_2	14·1010	− 0·46	− 0·85	—	− 1·13	− 2·02	− 5·85
,, ...	9·4840	+ 0·37	− 0·05	—	− 0·53	− 1·26	− 3·95
,, ...	4·7470	+ 0·42	+ 0·10	—	+ 0·10	+ 0·42	− 2·64
,, ...	2·8012 †	+ 0·8	+ 1·16	—	+ 0·98	—	− 1·51

* Corrected values: experimentally determined with (+)-ester. † $l = 4$.

Optically pure αγ-diethylallyl alcohol has a much larger optical rotatory power than its dimethyl analogue; moreover, the value of the rotation is far less affected by change of temperature (see Table II) than is that of αγ-dimethylallyl alcohol.

Although (+)-αγ-dimethylallyl alcohol undergoes rapid but erratic mutarotation (*loc. cit.*) involving a change in the sign of the rotatory power, yet the rotation of (+)-αγ-diethylallyl alcohol decreases only slowly with time, a 25% loss occurring in 17 months (Table III). It has not been possible to determine whether this loss of rotatory power is due to mutarotation and/or racemisation owing to the slow nature of the change.

TABLE II.

Observed Rotatory Powers and Densities of (+)-αγ-*Diethylallyl Alcohol at Various Temperatures* (l, 0·5).

t.	d_4^t.	α_{6438}.	α_{5893}.	α_{5780}.	α_{5461}.	α_{5086}.	α_{4358}.
18·5°	0·8397	—	+5·59°	+5·96°	+6·81°	+8·10°	+12·25°
27	0·8326	+4·40°	5·21	5·65	6·40	7·65	11·95
33·5	0·8270	—	4·95	5·34	6·01	7·10	11·25
71·5	—	2·90	3·42	—	4·06	5·05	7·83
22 *	0·8368	4·85	5·38	5·90	6·60	7·80	12·35

* Recooled.

Since the unsaturated aldehyde used in the synthesis of αγ-diethylallyl alcohol was obtained by a method which may have given rise to a mixture of *cis*- and *trans*-isomers (production of a double bond by elimination of the elements of hydrogen bromide), an attempt was made to separate a solid derivative prepared from the aldehyde into two isomeric forms. Fractional crystallisation of *dl*-αγ-diethylallyl hydrogen phthalate from light petroleum gave, however, no indication of the presence of *cis*- and *trans*-isomers. In

addition, Kuhn and Grundmann (*Ber.*, 1937, **70**, 1897) do not record any evidence for the presence of isomeric forms of the aldehyde. Hence it is concluded that the Δ^{α}-pentenal is essentially homogeneous and is probably the *trans*-isomer. Similarly, purified commercial crotonaldehyde, produced by the removal of the elements of water from aldol, is considered by Blacet, Young, and Roof (*J. Amer. Chem. Soc.*, 1937, **59**, 608) to consist solely of the *trans*-isomeride.

TABLE III.

Effect of Time on the Rotatory Powers of (+)-*αγ-Diethylallyl Alcohol* (l, 0·5).

Time, months.	*t.*	α_{6563}.	α_{5893}.	α_{5780}.	α_{5461}.	α_{5086}.	α_{4358}.	% activity of orig. alcohol at *t*°.
0	18·5°	—	+5·59°	+5·96°	+6·81°	+8·10°	+12·25°	100
1·6	24	+3·98°	5·23	5·55	6·35	7·63	11·60	98
4	21	—	5·31	—	6·44	—	11·91	97
7	17	4·44	5·43	5·81	6·73	7·92	12·58	97
9	21	—	5·43	5·69	6·46	—	11·86	97
12	21	—	5·08	5·42	6·13	—	10·92	92
17	15	—	4·31	4·50	5·27	—	9·38	75

EXPERIMENTAL.

dl-*αγ-Diethylallyl alcohol* was prepared in 67—74% yields by the interaction of Δ^{α}-pentenal (Kuhn and Grundmann, *loc. cit.*) with ethylmagnesium chloride. It had b. p. 58—64°/13 mm. and 154—156°/760 mm., $n_D^{19°}$ 1·4384 (Found: C, 73·4; H, 12·5. $C_7H_{14}O$ requires C, 73·7; H, 12·4%).

dl-*αγ-Diethylallyl Hydrogen Phthalate.*—The *dl*-alcohol (17 g.) was added to a solution of phthalic anhydride (22·2 g.) in pyridine (15 g.) and heated for 1¾ hours on the water-bath. After the usual working up, there was obtained dl-*αγ-diethylallyl hydrogen phthalate* (30 g., 77% yield), which crystallised from light petroleum (b. p. 40—60°) in rhombs, m. p. 66—68° (Found: C, 68·6; H, 7·0; *M*, by titration with NaOH, 263. $C_{15}H_{18}O_4$ requires C, 68·7; H, 6·9%; *M*, 262).

(+)-*αγ-Diethylallyl Hydrogen Phthalate.*—Strychnine (68 g.) was added to a hot solution of the *dl*-hydrogen phthalate (53 g.) in acetone (1 l.), and a mass of crystals was deposited overnight. These were filtered off, and thrice recrystallised from acetone, affording strychnine αγ-diethylallyl phthalate (43 g.), m. p. 173—178°. This on decomposition gave the (+)-hydrogen phthalate (12 g.), $[\alpha]_{5461}$ + 18·7° (*c*, 4·6175), which on crystallisation from light petroleum was optically pure with m. p. 73—75° and $[\alpha]_{5461}$ + 19·3° (*c*, 4·4905). The rotations of this and the following ester relate to $l = 2$ in chloroform.

(−)-*αγ-Diethylallyl Hydrogen Phthalate.*—Decomposition of the more soluble fractions of the above strychnine salt yielded *l*- + *dl*-hydrogen phthalate (23 g.) with $[\alpha]_{5461}$ − 10·1° (*c*, 4·8050). After two recrystallisations from light petroleum, there was obtained the pure (−)-hydrogen phthalate with $[\alpha]_{5461}$ − 19·1° (*c*, 4·6245) and m. p. 73—75°. Further recrystallisation failed to raise either its m. p. or its rotatory power; their equivalence with those of the (+)-hydrogen phthalate renders it very probable that optical resolution is complete.

Equal amounts of the pure (+)- and (−)-hydrogen phthalic esters were melted together and allowed to resolidify; the resultant solid had m. p. 67—69°, *i.e.*, identical with that of the *dl*-ester.

(+)-*αγ-Diethylallyl Alcohol.*—The (+)-hydrogen phthalate (8·1 g.) was heated on the water-bath for ½ hour with 15 c.c. of 5N-sodium hydroxide. The product, after steam-distillation, was salted out and extracted with ether. The ethereal solution, after drying with potassium carbonate, yielded the (+)-alcohol (3·0 g., 85% yield); b.p. 154—156°, $\alpha_{5893}^{18·5°}$ + 5·59°, $\alpha_{5461}^{18·5°}$ +6·81°, $\alpha_{4358}^{18·5°}$ + 12·25° ($l = 0·5$). Hydrolysis with 5N-alcoholic potash gave a similar result. In each case, reconversion into the (+)-hydrogen phthalate resulted in a 90% retention of optical activity. The effect of time on the rotatory power of the (+)-alcohol is shown in Table III.

The interest and advice of Dr. J. Kenyon, F.R.S., and of Dr. M. P. Balfe are gratefully acknowledged, and thanks are due to the Government Grants Committee of the Royal Society and to Imperial Chemical Industries Ltd. for grants. The Department of Scientific and Industrial Research is thanked for a maintenance grant.

BATTERSEA POLYTECHNIC, LONDON, S.W. 11. [*Received, March 28th*, 1941.]

60. *Triterpene Resinols and Related Acids. Part XIII. Note on the Bromination of α-Amyranonyl Benzoate and β-Amyranonyl Acetate.*

By D. E. Seymour and F. S. Spring.

Treatment of α-amyranonyl benzoate and β-amyranonyl acetate with bromine gives *bromo-α-amyranonyl benzoate* and *bromo-β-amyranonyl acetate*, which on heating with acetic acid containing a trace of hydrobromic acid lose hydrogen bromide and yield *iso*-α-amyrenonyl benzoate and *iso*-β-amyrenonyl acetate respectively.

In Part VII (Seymour, Sharples, and Spring, J., 1939, 1075) it was shown that treatment of the saturated keto-ester α-amyranonyl benzoate with bromine led to partial dehydrogenation, giving the αβ-unsaturated keto-ester, *iso*-α-amyrenonyl benzoate. During the bromination we had observed the separation of a crystalline solid which gradually redissolved. We have now shown that this crystalline solid is *bromo-α-amyranonyl benzoate*, m. p. 177—178°. By effecting the bromination under suitable conditions, this bromo-ketone can be isolated in high yield. When it is heated in acetic acid containing a trace of hydrobromic acid, rapid evolution of hydrogen bromide occurs and the bromo-ketone is converted into *iso*-α-amyrenonyl benzoate (Seymour, Sharples, and Spring, *loc. cit.*).

In the same way the bromination of β-amyranonyl acetate (Picard, Sharples, and Spring, J., 1939, 1045) has been reinvestigated; under suitable conditions the primary product of the reaction, *bromo-β-amyranonyl acetate*, m. p. 273—274°, is obtained. This bromo-ketone is extremely unstable, profound decomposition occurring when it is heated to 60° in a vacuum. Boiling solutions of the bromo-ketone gradually decompose with evolution of hydrogen bromide, this decomposition being most marked in acetic acid. A solution of the bromo-ketone in this solvent decomposes at room temperature with formation of *iso*-β-amyrenonyl acetate, the reaction being considerably accelerated by warming.

Experimental.

Bromo-α-amyranonyl Benzoate.—A solution of α-amyranonyl benzoate (3 g.) in glacial acetic acid (64 c.c.) was treated with a solution of bromine in acetic acid (8%; 12 c.c.) at 60°. The bromine was rapidly absorbed and the crystalline bromo-ketone separated. The mixture was set aside for 30 minutes at room temperature, and the solid then collected, washed with acetic acid, and recrystallised twice from acetone, from which *bromo-α-amyranonyl benzoate* separated (1·6 g.) in cubes, m. p. 177—178° (decomp.), $[\alpha]_D^{20°} + 22·5°$ ($l = 1$, $c = 0·6$ in chloroform). The m. p. of the bromo-ketone remained constant at 177—178° on recrystallisation, but after drying in a vacuum at 80° for 5 hours over phosphoric oxide it was 197—198° (Found: C, 70·7; H, 8·6. $C_{37}H_{53}O_3Br$ requires C, 71·0; H, 8·5%).

iso-α-*Amyrenonyl Benzoate.*—A solution of bromo-α-amyranonyl benzoate (1 g.) in acetic acid (30 c.c.) containing 1 drop of a solution of hydrogen bromide in acetic acid (40%) was heated on the steam-bath for 2 hours. The solution was set aside overnight and treated with water, and the precipitated solid collected and washed with water. After three crystallisations from acetone–methyl alcohol (1 : 1) *iso*-α-amyrenonyl benzoate separated in perfectly formed octahedra, m. p. 211—212°. A mixture of this with the specimen previously described (m. p. 205—206°) melted at 209—211° (Found: C, 81·4; H, 9·6. Calc. for $C_{37}H_{52}O_3$: C, 81·6; H, 9·6%).

Bromo-β-amyranonyl Acetate.—A solution of β-amyranonyl acetate (2 g.) in glacial acetic acid (110 c.c.) containing 1 drop of a solution of hydrogen bromide in acetic acid (40%) was treated at 40° with a solution of bromine in acetic acid (23 c.c.; 3%), added as rapidly as the absorption would permit. When the addition was complete, the solution was immediately treated with excess of water, and the precipitated solid collected and crystallised from slightly aqueous acetone, care being taken to avoid prolonged heating of the solution. After four crystallisations *bromo-β-amyranonyl acetate* separated in prismatic needles, m. p. 273—274°, $[\alpha]_D^{27°} \pm 0°$ ($l = 1$, $c = 0·6$ in chloroform) (Found: C, 68·1; H, 9·1. $C_{32}H_{51}O_3Br$ requires C, 68·2; H, 9·1%).

iso-β-*Amyrenonyl Acetate.*—A solution of bromo-β-amyranonyl acetate (0·7 g.) in glacial acetic acid (17 c.c.) was heated on the water-bath for 2½ hours, hydrogen bromide being continuously evolved. The solution was set aside overnight and largely diluted with water, and

the precipitated solid collected. After five crystallisations from slightly aqueous acetone, *iso*-β-amyrenonyl acetate separated in plates, m. p. 286—287°, undepressed by the specimen described by Picard, Sharples, and Spring (*loc. cit.*) *Light absorption in alcohol:* Maximum at 2480 A.; $\varepsilon_{max.} = 10{,}000$.

THE UNIVERSITY, MANCHESTER. [*Received, May 8th*, 1941.]

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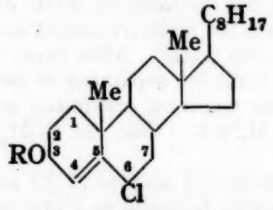
61. *The Conversion of 6-Chloro-3-benzoyloxy-Δ⁴-cholestene into Δ⁴:⁶-Cholestadienyl Benzoate.*

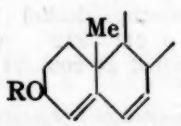
By F. S. SPRING and G. SWAIN.

Treatment of 6-chloro-3-benzoyloxy-Δ⁴-cholestene (I, R = COPh) with silver nitrate in pyridine gives *Δ⁴:⁶-cholestadienyl benzoate* (II, R = COPh) (with other products). Similar treatment of cholesterol dibromide gives a mixture of Δ⁴-cholestenone, 3 : 6-diketo-Δ⁴-cholestene, and an alcohol, m. p. 119—120°, benzoylation of which gives Δ⁴:⁶-cholestadienyl benzoate; acetylation of the alcohol gives Δ⁴:⁶-cholestadienyl acetate. The esters of Δ⁴:⁶-cholestadienol are stable and characterised by a single intense absorption maximum at 2390 A. The parent alcohol, however, is not stable to alkali.

WE have previously reported upon the dehalogenation of 6-chloro-3-benzoyloxy-Δ⁴-cholestene (I, R = COPh) (Spring and Swain, J., 1939, 1356) by means of potassium acetate in alcohol (*idem*, this vol., p. 83). In a further attempt to convert this substance into either Δ⁵:⁷- or Δ⁴:⁶-cholestadienyl benzoate, its behaviour with silver nitrate and pyridine (Dane, Wang, and Schulte, *Z. physiol. Chem.*, 1936, **245**, 80) has been examined. At room temperature, the reagent gave a mixture of a pyridinium salt, m. p. 158—159°, and the monobenzoate of *cis*-3 : 4-dihydroxy-Δ⁵-cholestene, m. p. 153—154°, identical with the product previously obtained by treatment of the 6-chloro-compound (I) with potassium acetate in alcohol. Treatment of (I, R = COPh) with the silver nitrate–pyridine reagent at 90°, on the other hand, gave a mixture of the pyridinium salt, m. p. 158—159°, the monobenzoate of the *cis*-diol, m. p. 153—154°, and a compound, m. p. 128—129°, which gave an intense yellow coloration with tetranitromethane in chloroform, a behaviour not observed with any of the other products obtained by dehalogenation of the 6-chloro-compound (I). The colour reactions, analysis and origin of the new compound, m. p. 128—129°, indicate that it is *Δ⁴:⁶-cholestadienyl benzoate* (II, R = COPh) and confirmation of this structure was found in its absorption spectrum, which exhibits a single maximum at 2390 A., $\varepsilon_{max.} = 33{,}000$.

(I.)

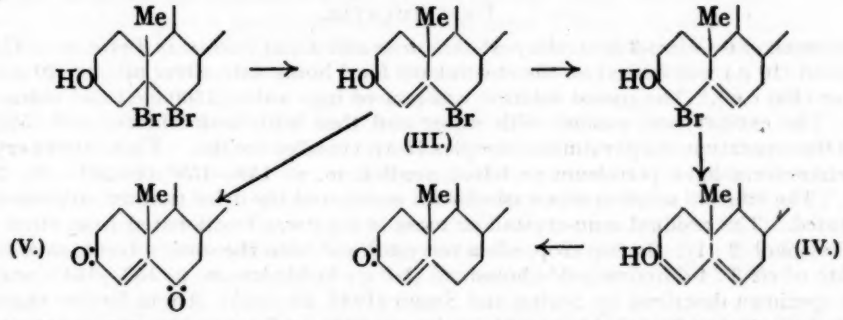




(II.)

Dane and Wang (*Z. physiol. Chem.*, 1937, **248**, 1) obtained an impure Δ⁴:⁶-cholestadienol (II, R = H) in small yield (*ca.* 4%) by treatment of cholesterol dibromide with silver nitrate in pyridine. This compound, m. p. 115—121°, gives an intense blue coloration with the antimony trichloride reagent; good analytical data could not be obtained for the free dienol. Dane and Wang ascribed the Δ⁴:⁶-structure to their product from a consideration of its origin, its colour reactions, and its absorption spectrum, but details of the latter are not given. In order to compare the Δ⁴:⁶-cholestadienol of Dane and Wang and its derivatives with the corresponding derivatives of Δ⁴:⁶-cholestadienol obtained from the 6-chloro-compound (I), the treatment of cholesterol dibromide with the silver

nitrate reagent was reinvestigated.* In our hands a large amount of ether-insoluble pyridinium complex was formed together with an ether-soluble resin, from which on long standing a small amount of solid separated; trituration of the resin with light petroleum as described by Dane and Wang did not prove a satisfactory method for the isolation of the dienol. The resin was successfully resolved into its components by solution in light petroleum and filtration through a column of aluminium oxide. The least heavily adsorbed fraction readily gave Δ⁴-cholestenone, which formed 50—60% of the ether-soluble resin. The formation of Δ⁴-cholestenone from cholesterol dibromide may be formulated as follows:



Alternative mechanisms are (*a*) the intermediate formation of Δ⁴·⁶-cholestadienol and its subsequent isomerisation to Δ⁴-cholestenone [*via* the enol-form (IV)] and (*b*) oxidation to 5:6-dibromo-3-ketocholestane, followed by debromination and isomerisation to Δ⁴-cholestenone.

The second component of the ether-soluble resin was obtained by continued washing of the chromatogram with light petroleum and was identified as 3:6-diketo-Δ⁴-cholestene (V), m. p. 121—122°. The formation of this diketone is probably to be attributed to the intermediate formation of 6-bromo-Δ⁴-cholestenol (III) and its subsequent oxidation, a reaction bearing a marked resemblance to the conversion of 7-bromo-6-ketocholestanyl acetate and 6-bromo-7-ketocholestanyl acetate into 6:7-diketocholestanyl acetate by means of the same reagent (Heilbron, Jones, and Spring, J., 1937, 801; Barr, Heilbron, Jones, and Spring, J., 1938, 334).

The most heavily adsorbed fraction of the ether-soluble resin was obtained in needles, m. p. 119—120°; this substance gives an intense blue coloration with the antimony trichloride reagent and a deep yellow coloration with tetranitromethane. It exhibits absorption maxima at 2395 A. and 2850 A.; repeated crystallisation did not achieve any alteration in the location or intensities of these maxima. This fraction contains a large proportion of Δ⁴·⁶-cholestadienol, since on benzoylation it readily gives Δ⁴·⁶-cholestadienyl benzoate, m. p. 128—129°, identical with the ester obtained by treatment of 6-chloro-3-benzoyloxy-Δ⁴-cholestene (I, R = COPh) with silver nitrate and pyridine, and exhibiting a *single* absorption maximum at 2390 A. ($\varepsilon_{max.}$ = 33,000). Likewise, acetylation of the fraction, m. p. 119—120°, gives Δ⁴·⁶-cholestadienyl acetate, m. p. 77—78°, $[\alpha]_D$ −67°, exhibiting a single absorption maximum at 2390 A., $\varepsilon_{max.}$ = 22,000, data in good agreement with those recorded by Petrow (J., 1940, 66) for the acetate (m. p. 78—79°; $[\alpha]_D$ −71·6°; $\lambda_{max.}$ 2390 A., $\varepsilon_{max.}$ ≏ 26,000) of Δ⁴·⁶-cholestadienol prepared by the reduction of Δ⁴·⁶-cholestadienone. Δ⁴·⁶·²²-Ergostatrienyl acetate, which contains the same major chromophor as Δ⁴·⁶-cholestadienyl acetate, exhibits an absorption maximum at 2400 A., $\varepsilon_{max.}$ ≏ 27,000 (Güntzel, *Ber.*, 1939, **72**, 1318).

Hydrolysis of Δ⁴·⁶-cholestadienyl acetate at 20° gave a product, m. p. 116—117°, $[\alpha]_D$ −34·9°, which exhibits a single absorption maximum at 2380 A., $\varepsilon_{max.}$ = 14,000. Hydrolysis of Δ⁴·⁶-cholestadienyl benzoate with boiling methyl-alcoholic potassium hydroxide, on the other hand, gave a product, m. p. 124—125°, which exhibits light absorption maxima at 2395 A., $\varepsilon_{max.}$ = 14,000, and at 2840 A., $\varepsilon_{max.}$ = 9000. Δ⁴·⁶-

* The experiments described in this paper were completed in October, 1939, prior to the appearance of a paper on Δ⁴·⁶-cholestadienol by Petrow (J., 1940, 66).

Cholestadienyl esters have not been hydrolysed to a substance with the properties expected of $\Delta^{4:6}$-cholestadienol; in the case of the hydrolysis product, m. p. 116—117° ("cold" hydrolysis), although it exhibits a single absorption maximum at 2380 A., the low intensity of this absorption compared with that of the parent $\Delta^{4:6}$-cholestadienyl acetate indicates that it is not pure $\Delta^{4:6}$-cholestadienol. The appearance of the absorption maximum at 2840 A., during the hydrolysis of $\Delta^{4:6}$-cholestadienyl benzoate ("hot" hydrolysis), may be due to partial dehydration to a cholestatriene. It is clear that $\Delta^{4:6}$-cholestadienol is not stable to alkali; Petrow (*loc. cit.*) has observed that the dienol is not stable to acids.

Experimental.

Treatment of 6-Chloro-3-benzoyloxy-Δ⁴-cholestene with Silver Nitrate in Pyridine.—The chloro-compound (10 g.) was heated on the steam-bath for 2 hours with silver nitrate (20 g.) and dry pyridine (400 c.c.). The cooled solution was poured into water (1500 c.c.) and extracted with ether. The extract was washed with water and then with hydrochloric acid (5%), which caused the separation of a pyridinium complex (2·5 g.) in silky needles. The complex crystallised from chloroform–light petroleum in felted needles, m. p. 158—159° (Found: N, 2·85; Cl, 4·8%). The ethereal solution was washed with water, and the dried (sodium sulphate) solution evaporated. The residual semi-crystalline mass (6·6 g.) was fractionated from ethyl acetate–methyl alcohol (2 : 1); the top crop, when recrystallised from the same solvent, gave the monobenzoate of *cis*-3 : 4-dihydroxy-Δ⁵-cholestene (1·1 g.) in blades, m. p. 153—154°, undepressed by the specimen described by Spring and Swain (1941, *loc. cit.*); it was further characterised by hydrolysis, the *cis*-3 : 4-diol being obtained, m. p. 176°, undepressed by an authentic specimen. Concentration of the mother-liquor from the top crop gave a more soluble fraction, which after several recrystallisations from ethyl acetate–methyl alcohol (2 : 1) gave *$\Delta^{4:6}$-cholestadienyl benzoate* (0·6 g.) in small prisms, m. p. 128—129°, $[\alpha]_D^{21°}$ −81° ($l = 1$, $c = 1·7$ in chloroform) (Found: C, 83·45; H, 10·0. $C_{34}H_{48}O_2$ requires C, 83·6; H, 9·9%). The benzoate gives an intense yellow coloration with tetranitromethane in chloroform and an intense blue coloration with the antimony trichloride reagent.

Treatment of Cholesterol Dibromide with Silver Nitrate in Pyridine.—Freshly prepared, dry cholesterol dibromide (48 g.) was added to a solution of silver nitrate (110 g.) in pyridine (600 c.c.) at room temperature. When solution was complete, the mixture was set aside for 5 days with exclusion of light. Ether (approx. 2 l.) was added to the solution until no further precipitation of silver salts and pyridinium compounds occurred. The separated solids were removed, and the ethereal solution washed with dilute hydrochloric acid (5%) and aqueous sodium carbonate (5%). Removal of the solvent from the dried (sodium sulphate) extract yielded a brown resin (15 g.), which was dissolved in light petroleum (b. p. 40—60°; 100 c.c.), and the solution filtered through a column of aluminium oxide (1″ diam., 10″ long). The chromatogram was developed by washing with solvents, and the following fractions collected:

Fraction.	Solvent.	Residue after removal of solvent.	Colour with antimony trichloride.
I	Light petroleum (100 c.c.)	Cryst. solid (5·1 g.)	Yellow-brown
II	,, ,, (200 c.c.)	,, ,, (0·95 g.)	,,
III	,, ,, (300 c.c.)	,, ,, (0·40 g.)	Yellow
IV	,, ,, (600 c.c.)	Part. cryst. (0·55 g.)	Green-yellow
V	Benzene–light petroleum (1 : 3) (100 c.c.)	,, ,, (0·05 g.)	Green
VI	,, ,, ,, (1 : 3) (600 c.c.)	Resinous solid (1·55 g.)	Green-blue
VII	Benzene (200 c.c.)	,, ,, (0·7 g.)	Blue

Δ⁴-Cholestenone.—Recrystallisation of fractions I and II from acetone–methyl alcohol (2 : 1) gave Δ⁴-cholestenone in prismatic needles, m. p. 80—81°, undepressed by an authentic specimen. The semicarbazone separated from 95% acetic acid in needles, m. p. 223—224° (decomp.), either alone or when mixed with an authentic specimen.

3 : 6-Diketo-Δ⁴-cholestene.—Fraction III separated from light petroleum in slightly yellow needles, m. p. 105—110°. After two recrystallisations from the same solvent this gave 3 : 6-diketo-Δ⁴-cholestene, m. p. 121—122°, undepressed by an authentic specimen (Found: C, 81·3; H, 10·5. Calc. for $C_{27}H_{42}O_2$: C, 81·4; H, 10·55%). Fraction IV proved to be mainly 3 : 6-diketo-Δ⁴-cholestene, but the purification of the diketone from this fraction was much more difficult to achieve than in the case of fraction III; fraction V was not examined.

$\Delta^{4:6}$-Cholestadienyl Acetate.—The aluminium oxide was divided into four sections, A, B, C, and D (lengths 1″, 2½″, 3″, and 3½″ commencing from the top). Section A was not examined;

the remaining three sections were eluted with acetone; removal of the solvent yielded the following fractions:

Fraction.	Residue (after removal of acetone).	Colour with antimony trichloride.	Colour with tetranitromethane.
B	Resin (0·75 g.)	Intense blue	Intense yellow
C	Oily solid (1·2 g.)	,, ,,	,, ,,
D	,, ,, (2·2 g.)	,, ,,	,, ,,

Fractions VI and VII, B, C, and D were combined and crystallised thrice from methyl alcohol to give a compound in small needles, m. p. 119—120°, $[\alpha]_D^{20°}$ −27·4° ($l = 1$, $c = 0·8$ in chloroform). Analysis gave a persistently low carbon value (Found: C, 83·3; H, 11·7. Calc. for $C_{27}H_{44}O$: C, 84·4; H, 11·5%). It gives an intense blue coloration with antimony trichloride and an intense yellow coloration with tetranitromethane in chloroform. *Light absorption in alcohol*: Maxima (*a*) 2395 A., $\varepsilon_{max.} = 12{,}500$; (*b*) 2850 A., $\varepsilon_{max.} = 12{,}000$. Acetylation of this compound (0·2 g.) was effected by refluxing for 45 minutes with pyridine (1·5 c.c.) and acetic anhydride (1·5 c.c.). The solution was diluted with water, and the product isolated by means of ether. Removal of the ether and crystallisation of the residue from ethyl acetate–methyl alcohol (1 : 1) gave $\Delta^{4:6}$-cholestadienyl acetate in needles, m. p. 77—78°, $[\alpha]_D^{20°}$ −67° ($l = 1$, $c = 1·0$ in chloroform); it gave an intense blue solution with antimony trichloride in chloroform and a deep yellow solution with tetranitromethane in chloroform. A mixture of the dienyl acetate with Δ^4-cholestenone enol-acetate (m. p. 79°) had m. p. 74° (Found: C, 81·7; H, 11·0. Calc. for $C_{29}H_{46}O_2$: C, 81·7; H, 10·8%).

$\Delta^{4:6}$-Cholestadienyl Benzoate.—The product, m. p. 119—120°, described above (0·3 g.) was heated on the steam-bath for 45 minutes with pyridine (2 c.c.) and benzoyl chloride (2 c.c.). The mixture was poured into aqueous sodium bicarbonate and extracted with ether; the product was thrice crystallised from ethyl acetate–methyl alcohol (2 : 1), from which $\Delta^{4:6}$-cholestadienyl benzoate separated in small prisms, $[\alpha]_D^{17°}$ −75° ($l = 1$, $c = 1·2$ in chloroform), m. p. 128—129°, undepressed by the specimen obtained from 6-chloro-3-benzoyloxy-Δ^4-cholestene.

Hydrolysis of $\Delta^{4:6}$-Cholestadienyl Acetate.—The acetate (1·0 g.) in absolute methylated spirit (50 c.c.) was treated with alcoholic potassium hydroxide (50 c.c.; 2%) solution at room temperature, and the mixture set aside for 70 hours. Water (250 c.c.) was added, and after standing for 1 hour at 0°, the crystalline precipitate was collected, washed with water, and recrystallised from methyl alcohol, from which the product separated in plates, m. p. 116—117°, $[\alpha]_D^{18°}$ −34·9° ($l = 1$, $c = 0·8$ in chloroform). Analysis again gave a low carbon value.

Hydrolysis of $\Delta^{4:6}$-Cholestadienyl Benzoate.—The benzoate (0·35 g.) was refluxed with methyl-alcoholic potassium hydroxide solution (20 c.c.; 3%) for 2 hours. The product was crystallised from methyl alcohol to give an alcohol, m. p. 124—125°, which gave an intense blue coloration with the antimony trichloride reagent and an intense yellow solution with tetranitromethane in chloroform. The carbon value was again low. The product became slightly yellow on exposure to light and air, and after three weeks the m. p. was 80—85°.

Grateful acknowledgment is made to Imperial Chemical Industries Limited (Dyestuffs Group) for the award of a Scholarship (to G. S.) and to Dr. A. E. Gillam for the absorption spectra data.

THE UNIVERSITY, MANCHESTER. [*Received, May 8th*, 1941.]

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62. *The Action of Organo-alkali Compounds on Benzonitrile.*

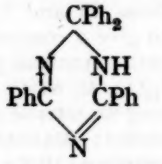
By R. M. ANKER and A. H. COOK.

The reaction between benzonitrile and a number of alkali alkyls, aryls, and aralkyls in ether and other inert solvents at room temperature has been examined. With a sufficiency of nitrile the products are either triphenylalkyldihydrotriazines or polyphenylpyrazolines. Products of the first type which contain a primary alkyl group liberate ammonia on heating to comparatively low temperatures. The products of this novel decomposition are 2 : 4 : 6-triphenylpyrimidines, rational syntheses of which have been effected. The production of these pyrimidines establishes the structure of the parent compounds as 1 : 3 : 5-triazines. The mechanism of these reactions is

discussed and reasons are advanced for the formation sometimes of pyrazolines, sometimes of dihydrotriazines.

In a recent paper (Cook and Jones, this vol., p. 278) it was noted that the action of sodium on benzonitrile in hot benzene led to the formation of sodium cyanide and good yields of 2 : 2 : 4 : 6-tetraphenyl-1 : 2-dihydro-1 : 3 : 5-triazine (I). The only feasible mechanism for the formation of (I) involves the intermediate formation of phenylsodium, which then exerts a polymerising and additive action on more benzonitrile:

$$PhCN + 2Na = NaPh + NaCN;\ NaPh + 3PhCN \longrightarrow$$



(I.)

If this were the mechanism, the additive and polymerising stage would be expected to take place at lower temperatures and only the first stage should necessitate a raised temperature. Thus, by working with preformed alkali alkyls, aryls, and aralkyls, further representatives of a group of heterocyclic compounds hitherto largely unexplored should become available. This paper describes the action of methyl-, ethyl-, propyl-, *iso*propyl-, butyl-, phenyl, and benzyl-lithium, and sodiodiphenylmethane on benzonitrile.

It being postulated that the action of alkali compounds would simulate that of other organo-metallic compounds, the products of these reactions might well have been kyaphenine—the tripolymeride of benzonitrile—or ketones resulting from intermediate imines. Diethylzinc (Frankland and Evans, J., 1880, **37**, 563) and sodiophenyl*cyclo*hexylmethane (Neunhoeffer and Nerdel, *Annalen*, 1936, **526**, 47) lead to kyaphenine and many examples of the formation of ketimines from Grignard reagents are known. We showed that in boiling inert solvents the action of Grignard reagents also is often a simple polymerising one leading to kyaphenine. A number of irregular results such as the formation of pyridines and pyrazolines (Ectors, *Bull. Acad. roy. Belg.*, 1923, **9**, 501) have been reported and bases of unknown nature (see, for example, Frankland, *loc. cit.*) have been obtained. With primary and secondary nitriles these irregularities become very numerous and difficult to formulate; they undoubtedly arise from participation of the hydrogen atoms attached to the carbon atom adjacent to the nitrile group and for this reason we restricted ourselves to benzonitrile.

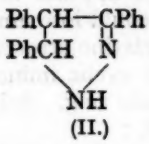
At room temperature in ether or benzene, only sodiotriphenylmethane of the alkali compounds examined exerted a simple polymerising action on benzonitrile; the reaction with metallic lithium was also mere polymerisation. In only one instance, the interaction of phenyl-lithium and benzonitrile, was any ketonic product obtained and even here the yield of ketone was very small. With these minor exceptions all the other reactions may be formulated as the formation of ketimines with subsequent addition of one or two more molecules of nitrile:

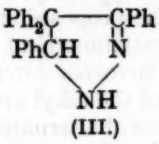
(i) $PhCN + LiR = Ph{\cdot}C(:NLi)R$
(ii) $Ph{\cdot}C(:NLi)R + PhCN = 2PhCN,RLi$
(iii) $Ph{\cdot}C(:NLi)R + 2PhCN = 3PhCN,RLi$

Bergmann (J., 1936, 412) treated benzonitrile with sodiodiphenylmethane and obtained the ketone $CHPh_2{\cdot}COPh$. We also have prepared this ketone indirectly, but our primary product of this interaction, a product which could be isolated in theoretical yield, was quite different (see below); it was obtained when the alkali compound was added to the nitrile even in equimolecular proportion.

The products containing two molecules of nitrile, that is, one molecule in addition to that which primarily forms ketimine, presented little difficulty. Such were obtained from benzyl-lithium and from sodiodiphenylmethane. The former was identical with the product of the action of benzylmagnesium chloride on benzonitrile which Ectors (*loc. cit.*) showed to be 3 : 4 : 5-triphenylpyrazoline (II). Its behaviour was closely parallelled by that of the product from sodiodiphenylmethane. This was likewise basic,

very stable towards hot acids, readily brominated in cold chloroform, and its ultra-violet absorption spectrum was practically identical with that of (II); lastly, it was oxidised


(II.)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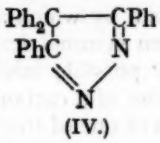
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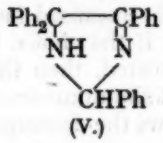
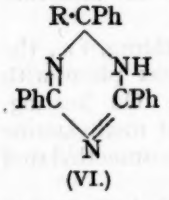

(V.)

by chromic acid to a compound containing two hydrogen atoms fewer than the parent. It was therefore formulated analogously as **3 : 4 : 4 : 5-*tetraphenylpyrazoline*** (III) and its oxidation product as the corresponding ***pyrazole*** (IV). Clearly its stability towards hydrolysing agents precluded all but cyclic structures; the only alternative, tetraphenyldihydroglyoxaline (V), which would also afford a cyclic oxidation product (tetraphenylglyoxaline), was rendered highly improbable by the product of ring-fission. The adduct was quite resistant towards acid and alkaline reagents, but when it was subjected to acetylating treatment a yellow intermediate was obtained; by boiling this with water, the colour disappeared and a non-nitrogenous ketone was obtained identical with that prepared by Bergmann (*loc. cit.*). The fission of dihydroglyoxalines on attempted acylation is not unknown (see, for example, Japp and Moir, J., 1900, **77**, 634), but the product of such fission is always an acylated base.

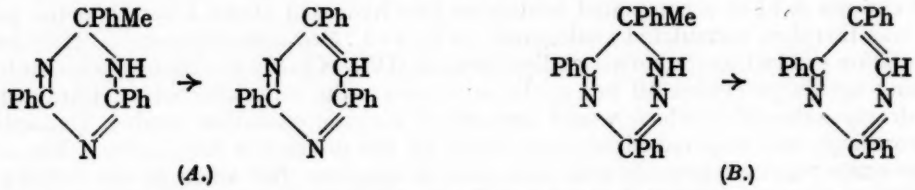
We attempted to synthesise these pyrazolines by adding diphenyldiazomethane to stilbene and to triphenylethylene in inert solvents. Unfortunately the diazo-compound failed to add to the olefin on gentle warming or irradiation in a mixture of benzene and light petroleum; this fact need occasion little surprise, however, when it is recalled that in such additions less heavily substituted olefins are usually more reactive. It was remarkable, therefore, that diphenyldiazomethane added quite readily to stilbene to give **3 : 3 : 4 : 5-*tetraphenylpyrazoline*** isomeric with the compound obtained from sodiodiphenylmethane. It showed the same characteristic of giving yellow solutions, particularly when hot, although the solid compounds were colourless.

Methyl-, ethyl-, propyl-, *iso*propyl-, butyl-, and phenyl-lithium with benzonitrile all gave products of the empirical form 3PhCN,RH; with the exception of a little benzophenone from phenyl-lithium, these were the only compounds found. The product from phenyl-lithium was identical with (I). If the course of the reaction with other alkyllithiums were similar, the products would again be dihydrotriazines (VI, R = Me, Et, etc.). This constitution was supported by the facts that the compounds were all similar strong bases forming crystalline salts; the methyllithium product was converted into a ***mono*-p-*toluenesulphonyl*** derivative, which was insoluble in caustic alkali as the derivative of a secondary base should be; on treatment with nitrous fumes it was converted into a product with the properties of an N-***nitroso***-compound; the absorption spectra of all these products were strikingly similar among themselves, but differed markedly from those of the pyrazolines mentioned above; finally, any likelihood of the products possessing acyclic constitutions was eliminated by their very great stability to permanganate, chromic acid, and hydrolysing agents. No ammonia was liberated by boiling with aqueous caustic potash and the compounds were only slowly attacked by boiling with 30% sulphuric acid, ketones being generated; the product from methyl-lithium, for example, afforded acetophenone. The only remaining alternatives are unsymmetrical dihydrotriazine structures (*e.g.*, as in scheme *B* below). Such constituents would, it is true, be in formal respects in accord with the products containing only two molecules of nitrile which have already been formulated as pyrazolines. Unsymmetrical dihydrotriazine structures were, however, eliminated by evidence from a quite unexpected direction.


(VI.)

The products from methyl-, ethyl-, *n*-propyl-, or *n*-butyl-lithium lost ammonia on heating to comparatively low temperatures (250—300°). The methyl-lithium product evolved almost exactly one molecule of ammonia and the residue, remarkably free from by-products, was a crystalline, very stable compound with the formula $C_{22}H_{16}N_2$. De-

composition of the other products was less satisfactory, but led to compounds with formulæ indicating that they were homologues of the C_{22} compound. There appears to be no well-recognised mechanism by which any of the proposed structures could lose ammonia, but if the choice between symmetrical and unsymmetrical dihydrotriazine structures be admitted, then the only possible mechanism involves extrusion of a cyclic imino-group and simultaneous inclusion of a carbon atom of the alkyl group into the ring. Scheme *B* shows the decomposition of one of the hypothetical alternatives to (VI):



It was thought significant as supporting this mechanism that elimination of ammonia only took place when the substituent R was a primary group containing two free hydrogen atoms as in the scheme; an acceptable explanation is thus provided of the difference between the propyl- and the *iso*propyl-lithium product, of which only the former furnished any ammonia on heating. If, now, the methyl-lithium product had structure (VI) (R = Me), its decomposition product could only be 2 : 4 : 6-triphenylpyrimidine; if it had one of the alternative structures, the decomposition product must be either 2 : 4 : 5-triphenylpyrimidine or an *o*- or *p*-diazine. Of these possibilities, only 2 : 4 : 6-triphenylpyrimidine had been prepared and this only by a series of reactions which could not be termed rational (Asahina and Kuroda, *Ber.*, 1914, **47**, 1819). The description of these workers' product agreed with ours except that they described the compound as "considerably soluble" in alcohol and 15% hydrochloric acid, whereas our product was sparingly soluble. On repeating Asahina and Kuroda's synthesis, we obtained a product which was certainly identical in every respect with our compound from benzonitrile. To remove all doubt we also synthesised 2 : 4 : 6-triphenylpyrimidine by an independent route. 6-Hydroxy-2 : 4-diphenylpyrimidine was converted into the 6-*chloro*-compound with phosphorus oxychloride and thence into triphenylpyrimidine with phenylmagnesium bromide. Again our first-mentioned product was identified with this authentic 2 : 4 : 6-triphenylpyrimidine. The primary product from methyl-lithium, then, has structure (VI) (R = Me).

On treatment of the primary product of the interaction of methyl-lithium, *i.e.*, the lithio-compound of (VI) (R = Me), with methyl iodide, methylation took place with formation of 2 : 4 : 6-*triphenyl*-1 : 2-*dimethyl*-1 : 2-*dihydro*-1 : 3 : 5-*triazine*. On heating, this *N*-methyl compound lost almost exactly one molecular proportion of methylamine to leave the same 2 : 4 : 6-triphenylpyrimidine as was obtained from the unmethylated base.

If thermal decomposition of the other alkyl-lithium products proceeded similarly and their structures were similar (VI, R = Et, Pr, or Bu), then the products should be 5-methyl-, 5-ethyl-, and 5-propyl-2 : 4 : 6-triphenylpyrimidine respectively. These three were synthesised by condensing the appropriate alkyl benzoylacetate with benzamidine at room temperature, converting the resulting 6-hydroxy-2 : 4-diphenyl-5-alkylpyrimidines into the 6-chloro-compounds, and thence with phenylmagnesium bromide, or in the case of the propyl homologue with phenyl-lithium, into triphenylalkylpyrimidines. The three pyrimidines were identical with the products from the dihydrotriazines. The suggested elimination of ammonia is thus confirmed, since groups which are introduced into the triazines as methyl, ethyl, propyl, and butyl finally appear in the pyrimidines as hydrogen, methyl, ethyl, and propyl respectively.

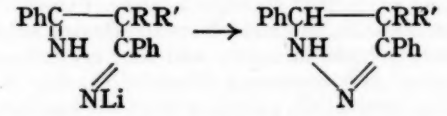
The mechanism of the reactions described here calls for at least one comment. It has been shown that the products are of the general form xPhCN,RH, where $x = 1$, 2, or 3. When $x = 3$, a triazine ring is formed with carbon and nitrogen atoms alternating in the ring, but when $x = 2$ two nitrogen atoms take up adjacent positions. The reason

for this difference, it is submitted, is that pyrazolines are formed only when the radical ·CHRR′ from which the alkali-metal compound is derived bears an activated hydrogen atom as in the benzyl and diphenylmethyl radicals. The first reaction stage is, as in other cases:

$$PhCN + CHRR'Li = Ph\underset{\underset{NLi}{\|}}{C}\cdot CHRR' \rightleftharpoons Ph\underset{\underset{NH}{\|}}{C}\cdot CRR'Li$$

(VII.) (VIII.)

Location of the alkali-metal atom will be governed by the relative acidities of the hydrogen atoms attached to the imino-nitrogen and to the radical ·CHRR′; when this radical is of the type under discussion, it may be assumed that in further reaction with benzonitrile the effective structure will be (VIII). Succeeding stages will not lead to structures with an alternation of carbon and nitrogen atoms in the ring, for the hypothetical intermediate succeeding (VIII) must be (IX), which will cyclise to (X)

(IX.)  (X.)

Elucidation of the constitutions of the above products was made more difficult by some unusual properties. Concordant analyses were only obtained when it became apparent that the compounds often crystallise from alcohol with one molecule of solvent which is retained with unusual tenacity. For example, the product from butyl-lithium crystallises as a monoalcoholate and loses no demonstrable proportion of alcohol even after 2 hours at 100° in a vacuum. The alcohol-free compound, and others like it, melted when recently fused at low temperatures, only to resolidify on further heating, finally melting at a comparatively high temperature. Neither this phenomenon nor the solvation appears, however, to be associated with chemical change, as it could be repeated indefinitely on the same sample.

Some less successful experiments deserve brief mention. No similar products were obtained from *p*-nitrobenzonitrile, and *o*-toluonitrile and methyl-lithium gave only an oily base. Reaction of alkyl-lithiums with phenylacetonitrile proceeded in a quite different direction, resulting in the formation of αβ-diphenylpropionitrile. Finally, in addition to the facts adduced by Linstead and Tuey (J., 1939, 1812) in connection with the formation of tetrabenztriazaporphin from methyl-lithium and phthalonitrile at a high temperature, we found in somewhat parallel experiments that a yield of 2% of pigment was obtained at the ordinary temperature in ether.

Experimental.

Note on the Preparation of Alkyl-lithiums.—For the present experiments the procedures of Gilman and collaborators (*J. Amer. Chem. Soc.*, 1932, **54**, 1957) and of Ziegler and Colonius (*Annalen*, 1930, **479**, 135) were modified. The preparations were carried out in a 3-necked nitrogen-filled flask fitted with stirrer and dropping-funnel; the third outlet led through a condenser and drying tube to a graduated bottle (1 l.) fitted with a 3-holed stopper, the other connections of which led to a nitrogen cylinder and through a syphon to a reservoir open to the air. The water level in the reservoir was arranged to be above that in the graduated bottle so as to maintain a slight excess pressure inside the apparatus. Connection was provided between the upper end of the condenser and the dropping-funnel so that the contents of the funnel flowed smoothly into the flask. On completion of the formation of the alkyl-lithium the stirrer was quickly replaced by a glass syphon fitted with a tap. The excess pressure in the apparatus then allowed the alkyl-lithium solution to be syphoned into benzonitrile.

The isolated yields of dihydrotriazines are not given, as they varied with the yield of alkyl-lithium and this depended on factors not easily controlled. As far as could be judged, the alkyl-lithium formed was converted quantitatively into dihydrotriazine.

2 : 4 : 6-*Triphenyl*-2-*methyl*-1 : 2-*dihydro*-1 : 3 : 5-*triazine*.—Methyl-lithium was prepared by adding to lithium (1·1 g.) under ether (60 c.c.), methyl iodide (4·4 c.c.) diluted with ether

(10 c.c.). About 60 drops of halide solution initiated the reaction, which was then maintained with ether refluxing without external heating; these details differ considerably from those mentioned by Gilman (*loc. cit.*). The resulting solution was syphoned into benzonitrile (30 g.); much heat was evolved and the solution was allowed to cool. Water was added, dropwise at first, and the ethereal solution dried and evaporated. Benzonitrile was recovered by distillation in a vacuum with the heating bath not above 150°; this precaution was necessary in view of the ready loss of ammonia. The residual *dihydrotriazine* solidified on cooling; it was recrystallised from ethanol, forming large crystalline clumps which sintered at 70°. Alcohol of solvation was expelled by careful fusion; the pure compound then melted at 62°, resolidified at 80—90°, and finally melted sharply at 143° (Found: C, 81·6; H, 5·6; N, 12·5. $C_{22}H_{19}N_3$ requires C, 81·3; H, 5·8; N, 12·9%). 2·5073 G. of solvated material lost 0·3198 g. on expulsion of ethanol of solvation; the apparent mol. wt. of the unsolvated material is thus 315 (calc. for $C_{22}H_{19}N_3$, 325) and the solvate must therefore be a monoalcoholate. When a solution of the free base was shaken with dilute sulphuric acid, the *sulphate* was precipitated. It was sparingly soluble in water, ethanol, or cold acetic acid, but crystallised from hot acetic acid. It decomposed at 251° but had m. p. 264° on rapid heating (Found: N, 9·8. $C_{22}H_{19}N_3,H_2SO_4$ requires N, 9·9%). The *hydrochloride*, prepared from an ethereal solution of the free base and hydrochloric acid, was readily soluble in acetic acid and crystallised with considerable loss from acetic acid–alcohol; m. p. 248° (decomp.) (Found: Cl, 9·5. $C_{22}H_{19}N_3$,HCl requires Cl, 9·8%). The p-*toluenesulphonyl* derivative, prepared from the free base and *p*-toluenesulphonyl chloride in pyridine and crystallised from aqueous alcohol, had m. p. 240—241° (Found: N, 8·7; *M*, cryoscopic in camphor, 460. $C_{29}H_{25}O_2N_3S$ requires N, 8·8%; *M*, 480). An alcoholic solution of the base, cooled in ice, was treated with nitrous fumes. The precipitate of N-*nitroso*-compound, crystallised from ethanol, had m. p. 205° (decomp.) (Found: N, 15·6. $C_{22}H_{18}ON_4$ requires N, 15·8%). It gave a positive Liebermann reaction.

The free dihydrotriazine (0·5095 g.) was heated to 300°; 0·0273 g. was lost and 30 c.c. of a basic gas were evolved. The gas therefore had an apparent $d = 20$ and could not have been methylamine. The residue was readily soluble in benzene, ether, or hot acetic acid, sparingly soluble in ethanol or cold acetic acid, and insoluble in water; crystallised from acetic acid, it had m. p. 184° (Found: C, 85·7; H, 5·2; N, 9·2. Calc. for $C_{22}H_{16}N_2$: C, 85·7; H, 5·2; N, 9·1%). It was identical in all respects with 2 : 4 : 6-triphenylpyrimidine synthesised by the method of Asahina and Kuroda (*loc. cit.*) and it was also synthesised independently. All attempts to condense benzamidine with dibenzoylmethane in presence or absence of caustic alkali or organic bases were unsuccessful. Benzamidine (4·1 g.) was condensed with ethyl benzoylacetate (5 g.) to yield 6-hydroxy-2 : 4-diphenylpyrimidine, m. p. 278° (6 g. or 90% of the theoretical) (cf. Pinner, *Ber.*, 1889, **22**, 1626). The hydroxy-compound was heated with excess of phosphorus oxychloride in a sealed tube overnight at 130°. Careful addition of water precipitated 6-*chloro*-2 : 4-*diphenylpyrimidine*, which was recrystallised from alcohol; m. p. 108° (6·0 g.) (Found: Cl, 13·0; N, 10·4. $C_{16}H_{11}N_2Cl$ requires Cl, 13·3; N, 10·5%). It was stable towards hydrolysing agents, withstanding the action of boiling aqueous caustic alkali apparently indefinitely. The chloro-compound (4 g.) was boiled with excess of phenylmagnesium bromide in toluene solution for 2 hours. The cooled solution was treated successively with alcohol, water, and dilute hydrochloric acid. The aqueous layer was extracted with ether, and the combined ether and toluene layers washed, dried, and evaporated. The residue solidified, was washed with a little ethanol, and recrystallised from acetic acid; it had m. p. 185° (yield, 4·0 g.) and was identical with the product of Asahina and Kuroda and with the product from benzonitrile.

The solution of lithiodihydrotriazine prepared as above was treated directly with methyl iodide (10 g.), and the whole refluxed for 2 hours in an atmosphere of nitrogen. On working up in the same manner, 2 : 4 : 6-*triphenyl*-1 : 2-*dimethyl*-1 : 2-*dihydro*-1 : 3 : 5-*triazine* was obtained in needles, m. p. 156°, crystallising from ethanol (Found: N, 12·4. $C_{23}H_{21}N_3$ requires N, 12·4%). The methylated base (185 mg.) was heated in a glass bulb to 300°, and the gas evolved aspirated through a saturated solution of picric acid in ether. Methylamine picrate (108 mg. or 87% of the theoretical yield), m. p. 205°, was collected; the bulb lost 18 mg. (calc. for the loss of 1 mol. of methylamine, 17 mg.) and the residue consisted of 2 : 4 : 6-triphenylpyrimidine, m. p. 185°.

2 : 4 : 6-*Triphenyl*-2-*ethyl*-1 : 2-*dihydro*-1 : 3 : 5-*triazine*.—Ethyl-lithium was prepared from lithium (0·8 g.), ether (60 c.c.), and freshly distilled ethyl bromide (4 c.c.) by the same procedure as was used for methyl-lithium. When the ethereal solution was syphoned into redistilled benzonitrile (15 g.), perceptible heat was evolved. The solid *dihydrotriazine* was

obtained on working up as in the case of the methyl analogue. It crystallised as an alcoholate from ethanol; alcohol was expelled by fusion before analysis, and the material then had m. p. 155° (Found: C, 82·0; H, 6·2; N, 12·2. $C_{23}H_{21}N_3$ requires C, 81·4; H, 6·2; N, 12·4%). It was readily soluble in benzene or ether, less so in alcohol.

The free base was fused at 200—300°. Considerable quantities of benzonitrile were evolved with ammonia. The residue was moistened with methanol, and the crystalline 2 : 4 : 6-triphenyl-5-methylpyrimidine recrystallised from ethanol or acetic acid; m. p. 178°. A mixture of equimolecular parts of ethyl methylbenzoylacetate (6 g.) and benzamidine hydrochloride (4·5 g.) in the minimum quantity of alcohol required to effect solution (*ca.* 20 c.c.) was treated with a slight excess of 10% caustic soda solution and kept at room temperature for 4 days. Dilute acetic acid was then added, and *6-hydroxy-2 : 4-diphenyl-5-methylpyrimidine* filtered off and recrystallised from acetic acid, forming needles (5 g.), m. p. 253° (Found: N, 10·7. $C_{17}H_{14}ON_2$ requires N, 10·7%). The latter was heated with excess of phosphorus oxychloride at 130° for 16 hours, and unchanged phosphorus halide decomposed with water; the insoluble *6-chloro-2 : 4-diphenyl-5-methylpyrimidine* crystallised from ethanol in needles (5 g.), m. p. 118° (Found: N, 10·0. $C_{17}H_{13}N_2Cl$ requires N, 10·0%). The chloro-compound was boiled with a large excess of phenylmagnesium bromide in toluene for 2 hours. On working up in the usual manner, 2 : 4 : 6-*triphenyl-5-methylpyrimidine*, crystallising from ethanol in needles, m. p. 182°, was obtained. It was identified with the former product, mixed m. p. 181° (Found: C, 86·0; H, 5·3; N, 8·6. $C_{23}H_{18}N_2$ requires C, 85·7; H, 5·6; N, 8·7%).

2 : 4 : 6-*Triphenyl*-2-n-*propyl*-1 : 2-*dihydro*-1 : 3 : 5-*triazine*.—*n*-Propyl-lithium was prepared in the same way as previous alkyl-lithiums from lithium (0·8 g.), redistilled *n*-propyl bromide (4·6 c.c.), and ether (50 c.c.). When the solution was syphoned into redistilled benzonitrile (15 g.), much heat was evolved. The solid dihydrotriazine was worked up in the usual manner; it crystallised from ethanol as an alcoholate readily soluble in benzene or ether. After expulsion of alcohol of crystallisation by fusion the *dihydrotriazine* melted at 50°, resolidified at *ca.* 78°, and melted again at 116° (Found: C, 82·1; H, 6·2; N, 11·9. $C_{24}H_{23}N_3$ requires C, 81·6; H, 6·5; N, 12·0%). The *sulphate* was obtained as with the lower homologue and crystallised from ethanol; m. p. 222° (Found: N, 9·0. $C_{24}H_{23}N_3,H_2SO_4$ requires N, 9·1%). The free dihydrotriazine was heated at 200—300°. The residue solidified when it was moistened with methanol; 2 : 4 : 6-triphenyl-5-ethylpyrimidine, crystallised from methanol or acetic acid, had m. p. 125°. Ethyl ethylbenzoylacetate and benzamidine hydrochloride were condensed as in the preceding examples. *6-Hydroxy-2 : 4-diphenyl-5-ethylpyrimidine* (yield, 4·5 g. from 7 g. of the keto-ester) crystallised from acetic acid in needles, m. p. 266° (Found: N, 10·3. $C_{18}H_{16}ON_2$ requires N, 10·1%). Treatment of the hydroxy-compound as before afforded *6-chloro-2 : 4-diphenyl-5-ethylpyrimidine*, which crystallised from ethanol in needles, m. p. 122° (Found: N, 9·2. $C_{18}H_{15}N_2Cl$ requires N, 9·4%). This was treated with excess of phenylmagnesium bromide in boiling toluene for 2 hours. 2 : 4 : 6-*Triphenyl-5-ethylpyrimidine* so obtained, and crystallised from methanol or acetic acid, had m. p. 127°. It was identical with the product of thermal decomposition of the dihydrotriazine above (Found: C, 85·6; H, 6·0; N, 8·2. $C_{24}H_{20}N_2$ requires C, 85·6; H, 6·0; N, 8·3%).

2 : 4 : 6-*Triphenyl*-2-iso*propyl*-1 : 2-*dihydro*-1 : 3 : 5-*triazine*.—The Grignard reagent prepared from magnesium (2·5 g.), *iso*propyl bromide (12·3 g.), and ether (60 c.c.) was syphoned into a suspension of lithium (1·7 g.) in ether (10 c.c.), and the whole refluxed for 3 hours. The *iso*propyl-lithium preparation was syphoned into benzonitrile (32 g.) and kept overnight. On cautious addition of water the *dihydrotriazine* was deposited; crystallised from alcohol, it had m. p. 184° (Found: C, 81·6; H, 6·8; N, 11·9; *M*, cryoscopic in camphor, 345. $C_{24}H_{23}N_3$ requires C, 81·6; H, 6·5; N, 11·9%; *M*, 353). It evolved no ammonia on heating to moderate temperatures.

2 : 4 : 6-*Triphenyl*-2-n-*butyl*-1 : 2-*dihydro*-1 : 3 : 5-*triazine*.—Lithium (0·8 g.), freshly distilled *n*-butyl chloride (5·2 c.c.), and benzene (50 c.c.) were warmed at 40—60° for 30 mins., and the tightly stoppered flask then shaken for 24 hours at room temperature. When the contents were syphoned into redistilled benzonitrile (20 g.), the mixture assumed a red colour and much heat was evolved. The *dihydrotriazine* was obtained in the usual manner. It was readily soluble in benzene or ether and crystallised from ethanol as a *monoalcoholate* (Found: N, 10·16. $C_{25}H_{25}N_3,C_2H_5{\cdot}OH$ requires N, 10·17%). After being freed from alcohol by fusion, it melted at 40—50°, resolidified at 60—70°, and finally melted sharply at 117° (Found: C, 81·5; H, 6·8; N, 11·6. $C_{25}H_{25}N_3$ requires C, 81·7; H, 6·8; N, 11·5%). The same compound was obtained by preparing *n*-butyl-lithium as in the preparation of methyl-lithium. The *sulphate*, crystallised from 30% methanol, had m. p. 215° (Found: N, 9·1. $C_{25}H_{25}N_3,H_2SO_4$

requires N, 9·0%). The *hydrochloride* was prepared by passing hydrogen chloride into a benzene solution of the free base and evaporating the solution to crystallisation; recrystallised from 50% ethanol, it had m. p. 256° (Found: N, 10·2. $C_{25}H_{25}N_3,HCl$ requires N, 10·4%). The hydrochloride was heated at 300—310° for 1 hour. The sublimate and residue were combined and crystallised from ethanol (charcoal). 2 : 4 : 6-Triphenyl-5-*n*-propylpyrimidine so obtained had m. p. 135°. No pyrimidine was obtained by heating the free base alone or with zinc chloride, such treatment leading only to the formation of kyaphenine.

Ethyl *n*-propylbenzoylacetate (7 g.), condensed with benzamidine hydrochloride (5 g.) as in previous examples, gave 6-*hydroxy*-2 : 4-*diphenyl*-5-n-*propylpyrimidine* (6 g.), which crystallised from acetic acid in needles, m. p. 235° (Found: N, 10·0. $C_{19}H_{18}ON_2$ requires N, 9·7%). As in earlier examples, it was converted in excellent yield into 6-*chloro*-2 : 4-*diphenyl*-5-n-*propylpyrimidine*, which formed needles from ethanol, m. p. 133° (Found: N, 9·2. $C_{19}H_{17}N_2Cl$ requires N, 9·1%). To an ethereal solution of the chloro-compound, an excess of ethereal phenyl-lithium solution was added. The excess was destroyed with water almost immediately, and the solution washed with water. The ether was removed, and the residual 2 : 4 : 6-*triphenyl*-5-n-*propylpyrimidine* crystallised from ethanol; m. p. 135° (Found: N, 7·9. $C_{25}H_{22}N_2$ requires N, 8·0%). It was identical with the product obtained from the butyldihydrotriazine above.

(*a*) Phenyl-lithium was prepared by dropping redistilled iodobenzene (10 g.) on lithium (0·7 g.) in ether (40 c.c.) and the solution was decanted through copper gauze into benzonitrile (15 g.). The usual procedure afforded 2 : 2 : 4 : 6-tetraphenyl-1 : 2-dihydro-1 : 3 : 5-triazine (3 g.), m. p. 192°; it was identified by direct comparison with the product of Lottermoser (*J. pr. Chem.*, 1896, **54**, 132). (*b*) Phenylmagnesium bromide in ether was treated with benzonitrile (10 g.; 3 mols.). After 5 minutes' boiling in ethereal solution, only benzophenone was obtained. The ether was replaced by xylene (25 c.c.), and the whole boiled for 4 hours. The cooled solution was treated with alcohol, and the precipitated kyaphenine (2·5 g.) removed. The filtrate, on standing, deposited the tetraphenyldihydrotriazine. Small yields of kyaphenine alone were obtained when methyl-, ethyl-, or propyl-magnesium iodide was used.

The Grignard reagent prepared from benzyl chloride (5·7 c.c.), magnesium (1·5 g.), and ether (30 c.c.) was decanted into a bottle containing finely cut lithium (2·5 g.), and the volume of ether made up to 250 c.c. The whole was shaken at room temperature for 11 days (the red colour was then at its maximum intensity), after which the residual lithium–magnesium alloy was allowed to settle, and the benzyl-lithium solution syphoned into benzonitrile (16 g.). The colour disappeared instantly and solid 3 : 4 : 5-triphenylpyrazoline was obtained as in previous reactions; crystallised from alcohol, it had m. p. 251° (Found: C, 86·4; H, 5·0; N, 8·9. Calc. for $C_{23}H_{16}N_2$: C, 86·2; H, 5·0; N, 8·8%). It was identical in every respect with the product of Ectors (*loc. cit.*).

3 : 4 : 4 : 5-*Tetraphenylpyrazoline.*—Sodiodiphenylmethane solution, prepared by shaking "molecular" sodium (1·4 g.) with benzhydryl methyl ether (6 g.) and ether (50 c.c.) overnight, was decanted into benzonitrile (9·5 g.). Some heat was generated and shaking was continued overnight. A few drops of water precipitated the *pyrazoline* in needles (9·6 g.); crystallised from benzene–light petroleum, it had m. p. 213° (Found: C, 86·6, 86·3; H, 6·2, 6·0; N, 7·5, 7·6. $C_{27}H_{22}N_2$ requires C, 86·6; H, 5·9; N, 7·5%). It was very soluble in warm acetic acid, benzene, or toluene, less soluble in alcohol, and it dissolved in dilute mineral acids. The pyrazoline was boiled for 13—15 mins. with acetic anhydride (3·5 c.c.), and the bright yellow solution decomposed with water. The insoluble colourless oil readily solidified and was recrystallised from 50% alcohol; it was identical with the ketone $C_6H_5{\cdot}CO{\cdot}CH(C_6H_5)_2$ obtained by Bergmann (*loc. cit.*) (Found: C, 88·0; H, 5·9. Calc. for $C_{20}H_{16}O$: C, 88·2; H, 5·9%). 3 : 4 : 4 : 5-Tetraphenylpyrazoline (1 g.) in acetic acid (10 c.c.) was treated with chromic acid (0·2 g.) in hot acetic acid (7 c.c.), and the whole boiled for 3 minutes. The solution was cooled and diluted with water, and the precipitate extracted with alcohol. The residual 3 : 4 : 4 : 5-*tetraphenylpyrazole* crystallised from acetic acid in highly refractive cubes, m. p. 175° (Found: C, 86·8; H, 5·7. $C_{27}H_{20}N_2$ requires C, 87·0; H, 5·4%). It gave colourless solutions, whereas the parent pyrazoline always gave yellow solutions which were deeply coloured when hot, although the solid compound was colourless.

3 : 3 : 4 : 5-*Tetraphenylpyrazoline.*—A solution of diphenyldiazomethane in light petroleum was treated with stilbene (1 mol.) in the minimum quantity of benzene, and the mixture irradiated before a mercury vapour lamp for 3 hours. The solution, after being evaporated until crystallisation commenced, was cooled; the deposit crystallised from alcohol to give 3 : 3 : 4 : 5-*tetraphenylpyrazoline*, m. p. 163° (Found: C, 86·8; H, 5·7; N, 7·4. $C_{27}H_{22}N_2$

requires C, 86·6; H, 5·9; N, 7·5%). Like its isomeride above, it gave coloured solutions, particularly when hot.

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63. *The Alkaloids of Bulgarian Belladonna Root.*

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The object of this investigation was the isolation of the individual alkaloids in the hope that the substance or substances responsible for the beneficial effects of Bulgarian belladonna root in certain nervous diseases might be identified. The alkaloids found have been *l*-hyoscyamine, *l*-hyoscine, tropine, and bellaradine. The last-named, which has not been found previously, is here described for the first time, has the formula $C_7H_{13}ON$ and is very soluble in water. It is a tertiary base containing a reduced pyrrole nucleus. Though our results have been obtained with a Bulgarian sample of belladonna, there is no reason to suppose that tropine and bellaradine would not be found in other samples of the root of any origin. There is no ground for a suggestion that either of these substances plays any part in the beneficial action of the drug in Parkinsonism, and their presence gives no support to the suggested superiority of the Bulgarian drug for this treatment.

EXTRACTS of belladonna and stramonium and the alkaloids therefrom have been commonly used in the treatment of paralysis agitans (Parkinsonism) for the last two decades. In 1935, however, Panegrossi (*Policlinico*, **2**, 56) drew attention to the striking results obtained by the use of Bulgarian belladonna root, which had been introduced by the herbalist Ivan Raeff of Chipka near Sofia. The essential feature of the so-called Bulgarian cure was the use of a decoction of Bulgarian belladonna root in white wine. Wines contain acid tartrates, and it seemed probable that the efficacy of the treatment might depend on the extracted alkaloids. It was therefore of importance that a thorough investigation of the alkaloids of Bulgarian belladonna root should be undertaken, to see whether any new bases were present to which the therapeutic activity could be ascribed.

It has long been known that the chief alkaloid of *Atropa belladonna* is *l*-hyoscyamine with a small but variable proportion of *dl*-hyoscyamine (atropine). Whether the atropine exists as such in the plant, or is produced in the process of isolation, is the subject of dispute. There appear to be but few authentic records of the occurrence of *l*-hyoscine in belladonna root. Schmidt (*Arch. Pharm.*, 1891, **230**, 207) records its isolation, but Klein and Sonnleitner (*Oesterr. Botan. Z.*, 1929, **78**, 9) failed to find it; Kuhn and Schäfer however (*Deut. Apoth. Ztg.*, 1938, **53**, 405, 424; *Münch. Med. Woch.*, 1938, 744) described its isolation and characterisation in two samples only, out of many examined. Of interest in connection with the present investigation are the observations of Goris and Larsonneau (*Bull. Sci. pharmacol.*, 1921, **28**, 499), who examined 500 kg. of belladonna leaves and found hyoscyamine, pyridine, 1-methylpyrrolidine and 1-methylpyrroline, and possibly 1 : 4-bisdimethylaminobutane. These findings are to some extent supported by the statement of Kuhn and Schäfer (*loc. cit.*), who claim to have found pyridine and 1-methylpyrrolidine in the roots if quantities of 5—10 kg. are used, but no details are given.

A Method for the Fractionation of Acids and Bases.—In the search for alkaloids which might be present in small proportions, a systematic process of exploration is required. In the solanaceous alkaloid group fractional precipitation or fractional crystallisation of the gold salts has hitherto been adopted for small quantities, but such methods have serious limitations. In 1920 one of the present authors (King, J., **117**, 991) used a method, for which no novelty was claimed, for separating bases which resisted other methods of fractionation. It made use of the differing basicities and avoided solubility relationships

of solid salts or sudden formation of precipitates. This method deserves wider recognition, since it has proved invaluable for the separation of mixtures not only of bases but also of acids (King, J., 1935, 1381; 1936, 1276; 1939, 1157) and lends itself to the separation of acids or bases on the micro-scale when they are present to the extent of a few milligrams. A convenient method of effecting the separation is to titrate the total isolated bases with a standard acid to neutrality and then to liberate the bases fractionally by addition of aliquot portions of standard alkali in the presence of an immiscible solvent such as ether or chloroform. If the mixture is thoroughly shaken, perfect equilibration is attained and the bases will be liberated to chloroform in the order of increasing basicity. Alternatively the bases in a suitable immiscible solvent are fractionally extracted with successive portions of standard acid, the strongest base being in this case removed first. The former method is usually the more advantageous, since the bases are isolated as such and are at all times under quantitative control.

In this communication, in order to isolate the alkaloids of belladonna root without the risk of change or racemisation, we have adapted the British Pharmacopœial assay process for belladonna alkaloids to larger scale operation. The use of an ammoniacal alcohol for extraction purposes excludes many undesirable plant constituents, which are taken out when an aqueous acid extracting medium is used. Although the use of ammonia means attaining a p_H of about 10, with consequent risk of racemisation of *l*-hyoscyamine if its action is prolonged, this has been avoided by reducing the time of contact with ammonia to a minimum. The use of cheap commercial alcohols in large volumes for extraction purposes involves the risk of introducing extraneous bases such as pyridine, and the use of large quantities of ammonia may also introduce traces of pyridine which would show up in the least basic fractions during subsequent fractionation of the alkaloids. For this reason we have distilled our methylated spirit (" methcol ") over tartaric acid, and the necessity for this precaution is shown by the fact that we have isolated pyridine, and identified it by salts, from the tartaric acid residue.

Isolation of l-*Hyoscyamine and* l-*Hyoscine.*—In applying the method of differing basicities to the alkaloids of belladonna root a difficulty arises, in that there are bases present whose distribution coefficient is in favour of the aqueous phase as against the chloroform phase. Such bases can only be extracted as a practical process in the presence of excess of concentrated alkali, and accordingly their subsequent fractionation has been effected by means of salts. The bases of belladonna root have therefore in this investigation been examined in two groups :—those extracted by chloroform in the presence of a saturated solution of sodium bicarbonate at p_H 8·5, and those extracted from concentrated caustic alkali at a p_H of 11 or over. In the former class the main alkaloid has been found to be *l*-hyoscamine without any significant proportion of atropine, and in the least basic fraction *l*-hyoscine has been found and characterised as its picrate and aurichloride. Hyoscine was only present to the extent of about 76 mg. in 9·9 kg. of root, but the method of fractionation employed has served to find it and to render its isolation a straightforward procedure.

Isolation of Tropine and Bellaradine.—The class of bases liberated at p_H 11 or over were neutralised with standard acid in the usual way, and then the bases were fractionally liberated by addition of aliquot portions of solid sodium bicarbonate. The remainder of the *l*-hyoscyamine, which had escaped extraction in the bases originally liberated by bicarbonate, was now readily separated in crystalline condition, but slightly racemised owing to the effect of the earlier treatment with concentrated alkali. Although the final solution was now saturated in respect of sodium bicarbonate, it still contained oily bases with a great affinity for water, and it needed addition of concentrated caustic alkali to facilitate their extraction. The optical rotation of this last fraction in neutral solution was practically zero. By fractionation of the mixture, as it proved to be, by means of the picrates, readily soluble tropine picrate was isolated. We consider that this base exists as such in belladonna root and has not been produced by hydrolysis. A much less soluble *picrate* of a new alkaloid, bellaradine, was also isolated to the extent of 0·75 g. from 9·9 kg. of root. Bellaradine has the formula $C_7H_{13}ON$ and the nitrogen atom is tertiary, since it adds on one molecule of methyl iodide to give ***bellaradine methiodide,***

which is a quaternary salt. A pyrrole nucleus is present, since the alkaloid gives the Runge pine-splinter reaction in typical fashion when heated with zinc dust, the process being suitably controlled by comparison with tropine and other alkaloids. Bellaradine is isomeric with nortropine and nor-ψ-tropine, but the secondary nature of the nitrogen atom in these alkaloids excludes identity of either with bellaradine. A specimen of nor-ψ-tropine, about which very little is known, was, however, prepared by epimerisation of the secondary alcoholic group of nortropine by sodium amyloxide. *Nor-ψ-tropine picrate*, like that of tropine and nortropine, proved to be a readily soluble salt, quite different from bellaradine picrate. A characteristic property of bellaradine is the ease with which it reduces the aurichloride to metallic gold. This behaviour is characteristic of ketones, such as tropinone and nortropinone in the tropane series, and also of granatonine and norgranatonine in the homotropane series. This property of bellaradine, and a consideration of the structure of the solanaceous alkaloids and of the coca alkaloids, suggested that the most likely structure for bellaradine might be 2-acetyl-1-methylpyrrolidine, that is, a lower homologue of hygrine, an alkaloid of Peruvian coca leaves. This base was synthesised (following paper) but proved to be different. The number of isomerides of $C_7H_{13}ON$ with a 1-methylpyrrolidine or 1-methylpyrrolidone structure is large, and an attempt will be made to characterise the function of the oxygen atom in bellaradine when more material is available. The possibility that the formula of bellaradine might be double that represented by $C_7H_{13}ON$ is not excluded. Attempts to determine the molecular weight were frustrated by the insolubility of the picrate and methiodide in camphor.

The quantity of bellaradine in Bulgarian belladonna root is so small that it is unlikely that the efficacy claimed for Bulgarian belladonna root is dependent upon its presence.

During these experiments on the isolation of hyoscyamine the rotation was frequently checked, the mercury green line of the spectrum being used as a source of light. As the ionic value of the specific rotation of *l*-hyoscyamine for the mercury green wave-length was apparently unrecorded, and it was necessary to know to what extent our hyoscyamine was contaminated with atropine, the preparation of optically pure *l*-hyoscyamine hydrobromide was undertaken. For this purpose *l*-hyoscyamine as isolated from belladonna root was crystallised as its *d*-camphorsulphonate following the method of Barrowcliff and Tutin (J., 1909, **95**, 1966). In attempting to recover *l*-hyoscyamine base from the pure camphorsulphonate without any risk of racemisation by alkali, sodium bicarbonate was used for the purpose of liberating the base. It was found, however, that under these conditions at a p_H of 8·5, chloroform only very partially extracted the free base, the main product in the chloroform being undecomposed *l*-hyoscyamine *d*-camphorsulphonate. Even at a p_H of 9·0, 20% of undecomposed camphorsulphonate came through into the chloroform. However, by neutralising the free base in this product with mineral acid, the *l*-hyoscyamine could be obtained free from camphorsulphonate by extracting the undecomposed *l*-hyoscyamine *d*-camphorsulphonate still present from the aqueous phase by chloroform. The *l*-hyoscyamine base could now be readily recovered pure from the solution of the hydrochloride and it crystallised readily. It gave a crystalline, very soluble, hydrated hydrobromide. The specific rotation of this was determined for the sodium and the mercury green line. The ionic values found for these lines were $[\alpha]^{20°}_{Na}$ — 32·4° and $[\alpha]^{20°}_{5461}$ — 40·3° respectively. The former is in exact agreement with the value given by Carr and Reynolds (J., 1910, **97**, 1332) and in good agreement with the figure $[\alpha]_D$ — 32·7° calculated from the rotation of *l*-hyoscyamine sulphate, $[\alpha]_D$ — 28·03°, given by Goris and Costy (*Bull. Sci. Pharmacol.*, 1922, **29**, 113).

Experimental.

Extraction of the Alkaloids of Bulgarian Belladonna Root.—9·9 Kg. of genuine Bulgarian belladonna root * (K. P. Shipkoff and Co., Kazanlik) were worked up by the following process. The drug was powdered in a drug mill to pass a 12-mesh sieve and batches of 1800 g. were kept moistened for 12 to 24 hours with 2 l. of 95% methcol. (This solvent may contain small amounts of pyridine bases; these were eliminated by distillation through a column over tartaric acid.) 2N-Ammonia (270 c.c.) was then added to the mixture and the contents, preferably in a stoppered vessel, were thoroughly mixed by shaking at intervals during 1 hour.

* 0·3% of hyoscyamine by the B.P. assay process.

The contents of the vessel were then tipped into percolators, extraction of the alkaloids being completed by percolation with a further 4 l. of methcol. The percolate was run directly into a mixture of water (20 c.c.), methcol (50 c.c.), and 32% hydrochloric acid (60 c.c.), added in 10 c.c. portions at intervals so as to limit the time of contact of the alkaloid with ammonia or with excess acid. The main percolation was carried out rapidly—4 l. of percolate should have come through within 90—120 minutes. The remainder was allowed to drain slowly and finally sucked off. The total volume of percolate per 1800 g. of root was about 5 l. The spirit was distilled off at or below 40° under reduced pressure: complete removal of spirit is desirable, as its absence facilitates later stages. The cooled aqueous fatty residue, which should be about 500 c.c., was filtered with suction through a thin layer of kieselguhr, the funnel being washed with a little ether. The filtrate was then extracted three times with ether and finally once with chloroform to remove fats, the ethereal and chloroform extracts being washed with small portions of N-hydrochloric acid to remove any alkaloids which were taken up. The final aqueous volume should be not more than 500 c.c.

The acid solution was then saturated with solid bicarbonate, the p_H being finally 8·5. The alkaloids were removed by repeated extraction with chloroform, as many as 12 extractions or more being needed to reduce the alkaloidal content of the aqueous liquor below a point at which a few drops, faintly acidified with mineral acid, no longer gave a turbidity with Tanret's reagent. The chloroform was distilled, baking on the sides of the flask being avoided and the last few c.c. of solvent being removed by a pump. The residue (*A*) readily crystallised if inoculated with *l*-hyoscyamine. Its fractionation is described below.

The parent aqueous liquor, which no longer gave a reaction with Tanret's reagent in acid solution, still gave a precipitate in neutral solution, a reaction indicative of more soluble alkaloids. The remaining alkaloids were obtained by addition of 50% sodium hydroxide solution (50 c.c.) corresponding to a p_H of about 10—11, followed rapidly by six extractions with chloroform. On removal of the solvent the residual bases (*B*) partially crystallised on inoculation with *l*-hyoscyamine.

5·5 Batches, each of 1800 g., were worked up as described above. The base in each case was neutralised to p_H 3 by N-hydrochloric acid, Congo paper being used as external indicator, and the specific rotations of the solutions were determined, dilution being necessary in some cases on account of the pigments present. The specific rotations in terms of the base were calculated on the assumption, which is less true for bases (*B*) than for bases (*A*), that all the bases were *l*-hyoscyamine, the concentration being deduced from the titre. The following values were obtained for the different batches:

Batch.		I.	II.	III.	IV.	V.	VI.
Bases (*A*) extracted at p_H 8·5	Titre, N/HCl	16·4	15·1	19·5	16·7	15·8	7·1 c.c.
	$[\alpha]_{5461}$	−43·9°	−50°	−37·1°	−41·4°	−43·1°	−39·7°
Bases (*B*) extracted at p_H 10—11	Titre, N/HCl	3·2	8·7	6·5	8·0	8·3	5·0 c.c.
	$[\alpha]_{5461}$	−15·3°	−17·6°	− 7·4°	−13·7°	−12·1°	−19·6°

Fractionation of the Bases (A) *extracted at* p_H 8·5.—The six neutral solutions of the p_H 8·5 extracts were combined and concentrated at room temperature over sulphuric acid to 115 c.c. Their total titre (see table) was 90·6 c.c. of N-hydrochloric acid, which corresponds to 7·6 g. of sodium bicarbonate. Accordingly, known weights of sodium bicarbonate were added so as to liberate the bases fractionally and the alkaloids were extracted at any one degree of acidity by shaking with three portions of chloroform, each of 50 c.c., since *l*-hyoscyamine is not readily extracted from aqueous solution by chloroform. Three fractions were collected after addition of separate portions of sodium bicarbonate, each of 1·9 g.; then seven fractions were collected after addition of separate portions of sodium bicarbonate, each of 0·4 g. The aqueous solution now had a p_H of 7·5 and 5·0 g. of sodium bicarbonate were added, followed by six extractions with chloroform. Each of these eleven fractions crystallised readily on inoculation with *l*-hyoscamine. (This confirmed the earlier findings in a preliminary pilot experiment using less material. Each fraction crystallised as *l*-hyoscyamine, which was identified in every fraction as the main constituent by its characteristic picrate and aurichloride.) The final solution was then treated with 25 c.c. of 50% sodium hydroxide solution, which raised the p_H to 11 and six chloroform extractions gave a little base (30 mg.), which partly crystallised as *l*-hyoscyamine. The first four fractions and the ninth fraction were neutralised with N-hydrochloric acid and required 8·8, 14·7, 16·17, 10·11, and 2·89 c.c.: the specific rotations of these fractions calculated in terms of the base were $[\alpha]_{5461}$ − 37·7°, − 39·5°, − 41·5°, − 43·7°, and − 40·5°, respectively. Fractions 2—9 were therefore almost pure

l-hyoscyamine, since any other alkaloid would be concentrated in the first least basic fraction or in the last more basic fractions. To confirm earlier preliminary findings, portions of fraction 4, $[\alpha]_{5461}$ — 43·7°, were converted into picrate and aurichloride. The picrate crystallised at first in tiny needles, which passed, when the solution was warmed, into plates, m. p. 164—165°. Barrowcliff and Tutin described the picrate as needles, m. p. 163° (J., 1909, **95**, 1977), whereas Carr and Reynolds (J., 1912, **101**, 950) describe it as rectangular plates, m. p. 165—166°. The aurichloride crystallised in leaflets and on one crystallisation from N-hydrochloric acid separated in deep golden-yellow leaflets, m. p. 167—168°. Barrowcliff and Tutin (*loc. cit.*) give m. p. 165°.

Isolation of l-*Hyoscine.*—Fraction 1, $[\alpha]_{5461}$ — 37·7°, required 8·8 c.c. of N-hydrochloric acid for neutralisation. The bases in it were fractionally liberated by addition of five successive portions of sodium bicarbonate, each of 0·15 g., followed by three extractions with chloroform at each stage. Finally, excess of saturated sodium bicarbonate solution (10 c.c.) was added, and the remaining base extracted. On removal of the solvent and inoculation with *l*-hyoscyamine, fractions 3, 4, 5, and 6 crystallised completely as *l*-hyoscyamine. Fraction 1 was a brown gum, and fraction 2 a brown oil which partly crystallised as *l*-hyoscyamine; their titres were 1·27 and 1·8 c.c. of N-hydrochloric acid respectively and their specific rotations in terms of the base $[\alpha]_{5461}$ — 26·0° and — 25·3°. These two fractions were therefore combined in the form of their hydrochlorides and refractionated by addition of ten successive portions of N/10-sodium carbonate, each of 3 c.c. Fractions 9 and 10 crystallised readily as *l*-hyoscyamine, but 1—8 showed no signs of crystallisation. Fraction 6 (about 0·1 g.) required 2·42 c.c. of N/10-hydrochloric acid to neutralise it and gave $[\alpha]_{5461}$ — 20·3° on the assumption that the equivalent of the base was that of hyoscine. Fractions 2—8 were now combined, neutralised with N/10-hydrochloric acid, and concentrated to 10 c.c. Of this, 5 c.c. were precipitated with saturated sodium picrate solution, and the remaining half with gold chloride solution. *l*-Hyoscine picrate (57 mg.) separated in a characteristic manner, a felt of slender needles which on crystallisation from water (2 c.c.) gave a salt, m. p. 165°, depressed by *l*-hyoscyamine picrate, which also melts at 165°, to 138° but not depressed by *l*-hyoscine picrate, m. p. 165—185°, freshly prepared from *l*-hyoscine hydrobromide of pharmacopœial quality. Pure *l*-hyoscine picrate melts at 187—188° (King, J., 1919, **115**, 476), but a specimen was not available for comparison.

The aurichloride was more satisfactory. It was obtained in 92 mg. yield and on crystallisation from N-hydrochloric acid (4 c.c.) separated in stout crystals, m. p. 205°, not depressed by *l*-hyoscine aurichloride, which also melted at 205°. Pure *l*-hyoscine aurichloride melts at 204—205° (King, *loc. cit.*), whereas the *dl*-form melts at 214—215°.

Fractionation of the Bases (B) *extracted at* p_H 10. *Isolation of Bellaradine.*—The total titre of these bases (see table) was 39·7 c.c. of N-hydrochloric acid, equivalent to about 3·4 g. of sodium bicarbonate. The combined solutions were evaporated over sulphuric acid in a vacuum to about 25 c.c. and the bases were liberated fractionally to chloroform by addition of 0·84 g., 1·68 g., and 0·84 g. of solid sodium bicarbonate, followed by 20 c.c. of saturated solution, bringing the p_H to 8·5, and finally by 25 c.c. of 50% sodium hydroxide solution. Three chloroform extracts were made at each stage. The titres and specific rotations (in terms of the base) of these five fractions, calculated on the assumption that the equivalent was that of hyoscyamine, were as follows:

Titre, N/HCl	5·78	6·71	3·45	3·25	18·49 c.c.
$[\alpha]_{5461}$	−35·5°	−38·5°	−16·9°	−4·5°	0·0°

Fractions 1 and 2 crystallised readily and were mainly *l*-hyoscyamine; fraction 3 crystallised partially as *l*-hyoscyamine. Fractions 4 and 5 were oils. Fraction 5 weighed about 2·5 g. and was optically inactive. The neutral solution of the hydrochloride of this last fraction was evaporated dry, and the residue crystallised from absolute alcohol and dry ether. The crystalline product obtained was not however uniform, so the bases were converted into the picrates and fractioned as such. There were two picrates present, a sparingly soluble one crystallising in minute balls on the walls of the vessel and a much more soluble one crystallising in rhombs which proved to be tropine picrate. It is now found that pure tropine picrate melts at 290—295°, whereas Willstätter and Iglauer (*Ber.*, 1900, **33**, 1173) give m. p. 275° (decomp.) (Found: C, 45·6; H, 5·1; N, 15·1. Calc.: C, 45·4; H, 5·0; N, 15·1%). The less soluble picrate was that of a new base, bellaradine. When pure, *bellaradine picrate* crystallises in small rods, m. p. 224—225° (decomp.), and requires 300 volumes of boiling water for its solution. The total quantity isolated was 0·75 g. (Found for different preparations: C, 44·0, 44·0, 43·7, 44·0, 44·2; H, 4·6, 4·7, 4·7, 4·6, 4·5; N, 16·1, 16·0, 16·0, 15·9. $C_7H_{13}ON,C_6H_3O_7N_3$

requires C, 43·8; H, 4·5; N, 15·7%). A portion of the picrates (about 0·68 g.) was converted into the hydrochloride, the picric acid being removed with ether. The final solution (about 20 c.c. in a 2 dcm. tube) showed a slight lævorotation, α_{5461} — 0·04°. The solution was evaporated dry, and the hydrochloride crystallised as a hygroscopic mass of needles. Very small test samples gave a crystalline aurichloride, m. p. about 189°, but attempts to prepare larger quantities for analysis always led to deposition of gold. The platinum salt was oily, as was the mercurichloride. No precipitate was obtained with perchloric acid. Treatment of an aqueous solution of the hydrochloride with sodium nitrite left the base unchanged, as was shown by recovery of the picrate. The base was regenerated from the hydrochloride by liberation with 50% sodium hydroxide solution and extraction with chloroform. It was an oil with a tropine-like odour and gave Runge's pine splinter reaction when heated with zinc dust. It was converted into the *methiodide* by boiling with methyl iodide in methyl-alcoholic solution. This quaternary salt was soluble in 40 volumes of boiling methyl alcohol and separated in compact clusters of crystals of indefinite shape, m. p. 253° (Found: C, 35·6, 35·7; H, 6·2, 6·1; N, 4·8, 5·0. $C_8H_{16}ONI$ requires C, 35·7; H, 6·0; N, 5·2%). The recrystallisation mother-liquors of the methiodide were distilled to a small volume, and 1 c.c. of water added, followed by 2 c.c. of saturated sodium picrate solution. The *methopicrate* separated in small needles, which on recrystallisation from 100 parts of boiling water separated in long orange needles, m. p. 228° with blackening (Found: C, 46·1, 45·9; H, 5·2, 5·1; N, 15·2, 15·4. $C_{14}H_{18}O_8N_4$ requires C, 45·4; H, 4·9; N, 15·1%).

Specific Rotation of the l-*Hyoscyamine Ion.*—The specific rotation of the *l*-hyoscyamine ion is according to Carr and Reynolds (J., 1910, **97**, 1332) — 32·4° for the sodium line. If Biot's law of inverse squares applied, this would correspond to — 37·6° for the mercury green line. As this value was far below those recorded above, it was necessary to determine the specific rotations of the *l*-hyoscyamine ion for the sodium and the mercury green line on a pure preparation of a salt not involving an optically active acid. For this purpose various fairly pure *l*-hyoscyamine hydrochloride liquors were combined, and the base recovered by means of sodium bicarbonate and chloroform. It was neutralised with Reychler's *d*-camphorsulphonic acid, and the *l*-hyoscyamine *d*-camphorsulphonate crystallised twice by addition of a large excess of dry ethyl acetate to a concentrated solution of the salt in hot absolute ethyl alcohol. Crystallisation was greatly facilitated by the use of an inoculum and for this we are indebted to Dr. T. A. Henry, Director of the Wellcome Chemical Research Laboratories. The pure salt crystallised in large prisms, m. p. 161—162° (Barrowcliff and Tutin, J., 1909, **95**, 1974, give m. p. 159°), and had $[\alpha]^{20°}_{5461}$ — 11·08° ($c = 0·6$) in water, whence $[\alpha]_{5461}$ for the *l*-hyoscyamine ion is — 42·8°, the value + 66·5° being assumed as the molecular rotation of the *d*-camphorsulphonate ion (Graham, J., 1912, **101**, 746). A second preparation *de novo* gave a product, m. p. 161—162°, and having $[\alpha]^{20°}_{5461}$ — 11·26°, whence $[\alpha]_{5461}$ — 43·2° for the basic ion. These values needed experimental confirmation on a salt not involving the use of an optically active acid.

For this purpose, 10·4 g. of pure *l*-hyoscyamine *d*-camphorsulphonate were dissolved in a little water and treated with sodium bicarbonate (2·5 g.; 1·5 mols.). The solution was extracted eight times with chloroform and on removal of the solvent the residual syrup only partially crystallised on seeding with *l*-hyoscyamine. On addition of 10 c.c. of N-hydrochloric acid (theoretical, 20 c.c.) the solution was strongly acid to Congo, showing that camphorsulphonic acid was present. The solution was therefore treated with saturated sodium bicarbonate solution (25 c.c.) and again extracted exhaustively with chloroform. The residue from the chloroform again crystallised only partially as *l*-hyoscyamine and contained camphorsulphonate (sulphur test). The mixture of base and salt was then treated with a mixture of saturated sodium carbonate (20 c.c.) and sodium bicarbonate (40 c.c.), which brought the p_H to 9. After repeated chloroform extraction and removal of the solvent the residue consumed 16 c.c. of N-hydrochloric acid, showing that there was about 20% of the original camphorsulphonate still present. The neutral solution was now extracted repeatedly with chloroform, which removed the *l*-hyoscyamine *d*-camphorsulphonate completely. On evaporation of the chloroform the residue readily crystallised on inoculation with this salt (yield, 2·7 g.). The aqueous solution of *l*-hyoscyamine hydrochloride was then saturated with sodium bicarbonate to p_H 8·5 and thoroughly extracted with chloroform. On removal of the solvent the *l*-hyoscyamine base now crystallised readily and completely in typical fashion. It was neutralised with hydrobromic acid and the solution was concentrated to a syrup, which deposited prisms of the hydrobromide containing two molecules of water of crystallisation (Found: loss on drying in a vacuum or at 100°, 8·0, 8·9. Calc. for $2H_2O$, 8·9%). The specific rotation of this very

soluble salt was determined in water, the sodium and the mercury green line being used, $[\alpha]^{20°}_{Na}$ $-32{\cdot}4°$; $[\alpha]^{20°}_{5461}$ $-40{\cdot}3°$ ($c = 0{\cdot}5$), whence rotatory dispersion $Hg_{5461}/Na_{yellow} = 1{\cdot}24$. Incidentally this confirms exactly the ionic value given by Carr and Reynolds for the sodium line and it also shows that the rotations do not follow Biot's simple inverse square law.

Preparation of Nor-ψ-tropine.—Through the kindness of Dr. W. Mitchell of Messrs. T. and H. Smith of Edinburgh some nortropine carbamate was available. Of this, 0·5 g. was added to a solution of sodium (1 g.) in boiling alcohol (b. p. 135°) and the clear solution was boiled for 3 hours. The solution was neutralised with 3N-hydrochloric acid and evaporated to dryness. The crude nor-ψ-tropine hydrochloride, which crystallised in plates, was extracted with absolute ethyl alcohol. The solvent was removed, replaced by a little water, and a slight excess of sodium picrate solution added. An oily picrate separated and partly crystallised after a short time in large prisms. *Nor-ψ-tropine picrate* was readily soluble in warm water and after two crystallisations separated in clusters of prisms, m. p. 187—188°, depressed to 150° by nortropine picrate (Found: C, 43·8; H, 4·7; N, 15·1. $C_7H_{13}ON,C_6H_3O_7N_3$ requires C, 43·8; H, 4·5; N, 15·7%). This picrate, like those of tropine and nortropine, was very much more soluble in water than bellaradine picrate and also crystallised in much larger crystals.

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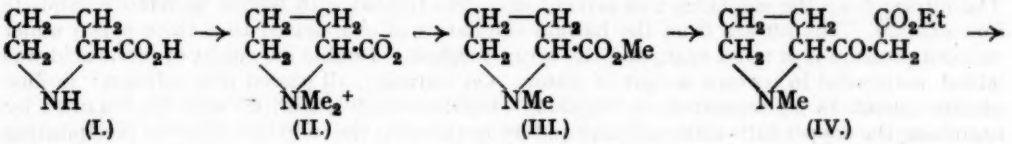
64. 2-*Acetyl*-1-*methylpyrrolidine*.

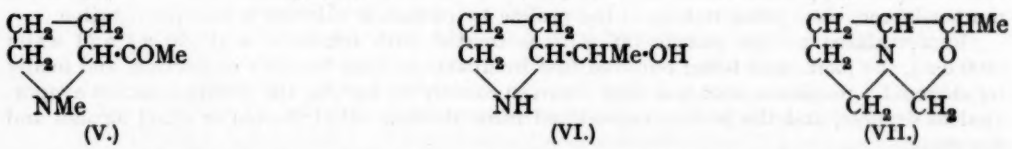
By HAROLD KING.

2-Acetyl-1-methylpyrrolidine has been synthesised from proline. It is different from bellaradine.

THE alkaloidal base, bellaradine, $C_7H_{13}ON$, was obtained from Bulgarian belladonna root, only in sufficient quantity to establish its composition with certainty and to show the presence of a pyrrolidine ring with a tertiary nitrogen atom (King and Ware, preceding paper). The most likely structure for such a base seemed to be that of 2-acetyl-1-methylpyrrolidine. The latter base has now been synthesised from proline (I) by conversion into the betaine stachydrine (II) and dry distillation of the latter with the formation of methyl hygrate (III). This ester was condensed with ethyl acetate in the presence of sodamide to yield ethyl 1-methylpyrrolidoyl-2-acetate (IV), which was not isolated but was hydrolysed with loss of carbon dioxide to form 2-acetyl-1-methylpyrrolidine (V).



(I.) (II.) (III.) (IV.)



(V.) (VI.) (VII.)

This substituted amino-ketone is an unstable substance which on keeping deposits a viscous oil having possibly a tricyclic structure. It can, however, be stabilised in the form of salts, the *aurichloride*, picrate and methopicrate being obtained crystalline. The properties of the base, its salts and derivatives are completely different from those of bellaradine.

Hess, Merck, and Uibrig (*Ber.*, 1915, **48**, 1900), by the action of formaldehyde at 120° in the presence of mineral acid on methyl-2-pyrrolidylcarbinol (VI), obtained a substance which they described as 2-acetyl-1-methylpyrrolidine (V). Hess, however, in a private communication to the editors of Beilstein's "Handbuch" (4th Edition, Supplementary

Vol., XXI, p. 263) considers this structure as doubtful and prefers to regard it as 5-methyl-3 : 4-trimethyleneoxalidine (VII). The latter structure is probably correct, since the properties of 2-acetyl-1-methylpyrrolidine now synthesised from proline are different from those of the base described by Hess and his collaborators. The following table gives a comparison of the properties of bellaradine, 5-methyl-3 : 4-trimethyleneoxalidine, and 2-acetyl-1-methylpyrrolidine :

	B. p.	Picrate, m. p.	Aurichloride, m. p.	Methopicrate, m. p.
Bellaradine	—	225°	189°?, unstable	228°
Methyltrimethyleneoxalidine	56—57°/26 mm.	175	—	—
2-Acetyl-1-methylpyrrolidine	75—80/30 mm.	118	108—109	202

Experimental.

Preparation of Proline.—For the preparation of this amino-acid Town's copper salt method (*Biochem. J.*, 1928, **22**, 1083; 1936, **30**, 1837) was applied with modification to gelatin, the purification of the proline and separation from hydroxyproline (compare Klabunde, *J. Biol. Chem.*, 1931, **90**, 293) being assisted by cadmium chloride precipitation as described by Kapfhammer and Eck (*Z. physiol. Chem.*, 1927, **170**, 299).

Gelatin (100 g. of Coignet's gold label) was dissolved in water (400 c.c.), sulphuric acid (200 g.) added, and the solution boiled for 6 hours. When cold, baryta (640 g. of octahydrate in 3 l. of water) was added until the reaction was neutral or faintly alkaline. The filtered solution was concentrated to a small bulk at 50° and digested on the water-bath with copper carbonate in excess. The filtrate was evaporated to a syrup, which was stirred with acetone, and the granular copper salts kneaded several times with fresh portions of dry acetone until they were obtained as a fine powder. This was quickly transferred to a dish and dried in a high vacuum over sulphuric acid. It was repowdered and redried in a vacuum and then finally in an oven at 110° for 2 hours. It was quickly transferred to a wide-mouthed stoppered bottle, allowed to cool, and treated, once only, with dry methyl alcohol (500 c.c.). The contents were kept for 24 hours with occasional shaking. The solution was then filtered, the methyl alcohol distilled off, the residue dissolved in water, and the copper removed as sulphide. The filtrate was evaporated to a syrup, and excess of ethyl alcohol added gradually to precipitate crude hydroxyproline, which often separated in the crystalline state. After removal of this crude hydroxyproline the filtrate was again evaporated to dryness and again treated with excess of ethyl alcohol to precipitate a further quantity of hydroxyproline. The alcoholic filtrate was then treated with a saturated solution of cadmium chloride in spirit so long as a precipitate formed. After a few hours the cadmium chloride–proline precipitate was collected and dissolved in water, saturated silver sulphate solution added in slight excess, and the filtrate from the silver chloride saturated with hydrogen sulphide to remove silver and cadmium ions. The filtrate from the sulphides was aerated and then treated with baryta to remove sulphate ions exactly. The filtrate from the barium sulphate was evaporated to a thick syrup under reduced pressure in a tared flask, and the syrup weighed. Double its weight of picric acid was added, suspended in its own weight of water. On warming, all passed into solution; proline picrate (about 18 g.) separated on standing. Further small quantities may be obtained by reworking the copper salts after redrying and by working up the cadmium chloride precipitation mother-liquor, since precipitation of the proline by cadmium chloride is not quantitative.

Recrystallised proline picrate (86 g.) was treated with sulphuric acid (20 g.) and water (200 c.c.), the picric acid being removed first by filtration, then by ether extraction, and finally by charcoal. Sulphuric acid was then removed exactly by baryta, the proline solution evaporated to dryness, and the proline crystallised from absolute ethyl alcohol or ethyl alcohol and dry ether.

Preparation of Stachydrine.—Proline (26 g.), methyl alcohol (270 c.c.), methyl iodide (43·5 c.c.), and sodium hydroxide (27 g.) were boiled under reflux for 6 hours. As the solution was still alkaline, a further quantity of methyl iodide (10 c.c.) was added and boiling was continued for a further 6 hours. The methyl alcohol was distilled off, and the residue dissolved in water and heated with excess of freshly precipitated silver chloride. The filtrate was evaporated to dryness, and the stachydrine hydrochloride extracted by absolute ethyl alcohol. It was obtained completely free from sodium chloride by a repetition of the process and crystallised readily in needles. It was dissolved in water and treated with freshly precipitated silver oxide to remove chloride ion, and the filtrate evaporated to dryness at room temperature over sulphuric acid in a vacuum. Hydrated stachydrine separated at first, but eventually

this was dehydrated to the anhydrous solid. Yield, quantitative. The gold salt melted at 231° in agreement with the highest m. p. recorded in the literature by Yoshimura (*Z. physiol. Chem.*, 1913, **88**, 338).

Methyl Hygrate.—The following process is an improvement on that given by Trier (*ibid.*, 1910, **67**, 328). 5 G. quantities of the perfectly anhydrous stachydrine, in a roomy flask with a low wide side-arm bent to serve as a receiver, were heated in a metal-bath to about 230°; effervescence then took place. When the temperature was then allowed to rise to 260°, methyl hygrate passed over as an almost colourless liquid (yield, 78%). The combined distillate from several experiments was redistilled and had b. p. 90°/18 mm., the first few drops being discarded, as they had a blackening effect on gold chloride solution. The main distillate gave methyl hygrate aurichloride, m. p. 85°; Trier (*loc. cit.*) gives m. p. 84—86°. The ester seemed to be the racemic form, since in a 1 dcm. tube the observed rotation for the mercury green line was + 0·04°.

Condensation of Methyl Hygrate with Ethyl Acetate. Preparation of 2-Acetyl-1-methylpyrrolidine.—Methyl hygrate (7·15 g.), dry ethyl acetate (4·4 g.), dry benzene (15 c.c.), and sodamide (2·0 g.) were boiled for 5½ hours, a clear solution being obtained. Hydrochloric acid (16%) was added in excess and after the benzene had been distilled off the contents of the flask were boiled until carbon dioxide was no longer evolved (about 2·5 hours). The solution was neutralised with 50% sodium hydroxide solution, made strongly alkaline by addition of a further 25 c.c., and repeatedly extracted with chloroform; on removal of this solvent by distillation a pale yellow oil (2·5 g.) was obtained. On keeping, it deposited a brown viscous oil which increased in quantity with time. Its formation was accelerated during the distillation of the base, which boiled at 75—80°/30 mm.

2-Acetyl-1-methylpyrrolidine, when dissolved in 3N-hydrochloric acid and treated with gold chloride solution, gave an oily gold salt which soon crystallised. The *aurichloride*, recrystallised from N-hydrochloric acid, formed small tablets, m. p. 108—109°. The solutions, unlike bellaradine gold chloride solution, showed no tendency to precipitate metallic gold [Found (micro-analyses): C, 17·5; H, 3·0; N, 3·7, 3·2, 3·5; Au, 42·5, 42·4, 41·8. $C_7H_{13}ON,HAuCl_4$ requires C, 18·0; H, 3·0; N, 3·0; Au, 42·2%]. The picrate separated as an oil from an alcoholic solution of the components, but crystallised on keeping and could then be recrystallised from water, from which it separated in plates, m. p. 118°. A portion of the base formed an oily methiodide on dissolving in methyl iodide, and on double decomposition with aqueous sodium picrate gave a crystalline methopicrate, m. p. about 202° (without decomp.).

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65. *Furanose and Pyranose Derivatives of Glucurone.*

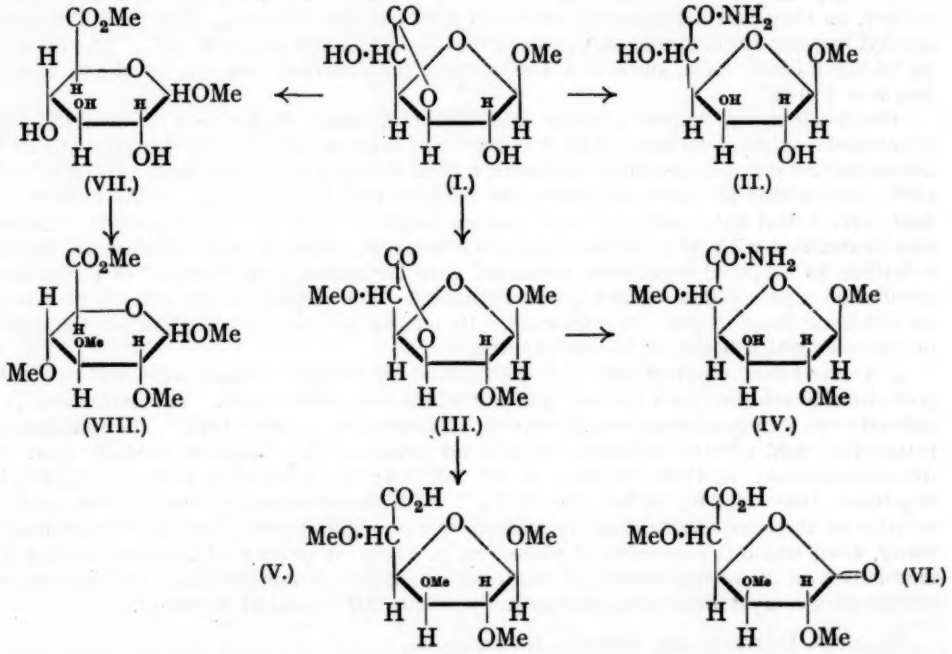
By L. N. OWEN, S. PEAT, and (in part) W. J. G. JONES.

A new derivative of methylglucopyruronoside is described and, in addition, derivatives of glucurone which have a furanose ring have been prepared. Glucurone (glucuronolactone) has been converted into the crystalline *γ-lactone* of *β-methylglucofururonoside* (I), the structure of which is proved by complete methylation, oxidation, and esterification to give the methyl ester of 2 : 3 : 5-trimethyl saccharolactone. From (I) has been prepared the *methyl* ester of *methylglucopyruronoside* (VII), which on complete methylation gives the methyl ester of 2 : 3 : 4-trimethyl methylglucuronoside (VIII). Crystalline 1 : 2-*monoacetone glucofururonolactone* (IX) has been obtained from glucuronolactone and also from 1 : 2-monoacetone glucofururonic acid (X) and it has been converted into the crystalline *amide* (XI); the latter has been prepared also from (X).

THE discovery of the presence of uronic acid residues in many polysaccharides of both plant and animal origin has awakened interest in the possibility of preparing derivatives of uronic acids which would be of value as synthetic agents. For this purpose it is sometimes desirable that such derivatives should be of the incompletely substituted type, in order that condensation with other compounds may take place through the remaining hydroxyl groups. Hitherto, all such products have been of the pyranose form; the

present communication is concerned with the formation of derivatives of glucuronolactone (glucurone) in which the sugar ring is of the furanose type.

The action of cold acid methyl alcohol on glucuronolactone led to the formation of a crystalline compound with the empirical formula $C_7H_{10}O_6$, containing one methoxyl group. Under the conditions of the reaction, the introduction of such a residue would be expected to occur only at the reducing carbon atom, C_1, with the formation of a glycoside, or at C_6 with the formation of an ester. Either view is supported by the fact that hydrolysis of the substance with hot dilute acid regenerated glucurone.



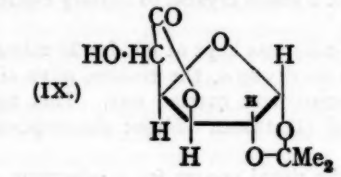
A methyl ester formed from glucurone would have the composition represented by the formula $C_7H_{12}O_7$ and it was evident, therefore, that the product was not an ester, a view which was substantiated by the stability of the methoxyl group towards hot alkali. By the following procedure the compound was shown to be the *γ-lactone* of β-*methyl-glucofururonoside* (I).

Methylation of (I) with Purdie's reagents gave the *γ-lactone* of 2 : 5-*dimethyl* β-*methyl-glucofururonoside* (III), which was converted with methyl-alcoholic ammonia into the crystalline *amide* (IV). Further methylation of (III) with methyl sulphate yielded 2 : 3 : 5-*trimethyl methylglucofururonoside* (V). Scission of the glycosidic methyl group, followed by oxidation with bromine, resulted in the formation of 2 : 3 : 5-trimethyl saccharolactone (VI), which on esterification gave the crystalline methyl ester of 2 : 3 : 5-trimethyl saccharolactone, identical with a specimen prepared by F. Smith (unpublished work). Furthermore, (I) was converted into a liquid *amide* (II), which gave a positive Weerman reaction for α-hydroxy-amides, thus providing additional evidence of the presence of a hydroxyl group at C_5.

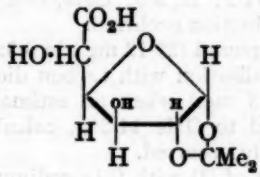
These observations showed clearly that (I) was in the furanose form, and rotational evidence suggested that the β-configuration should be assigned to the compound. In aqueous solution, (I) was neutral to litmus and showed no mutarotation, the behaviour in this respect resembling that of glucuronolactone. Titration with cold alkali followed the usual course for a γ-lactone, but the amount taken up was in excess of one equivalent. Furthermore, a reducing action was apparent when (I) was added to boiling Fehling's solution. An explanation of these anomalies is to be found in the presence of two five-membered rings in the molecule, since it is known that sugars containing double ring

systems readily give rise to unsaturated products which are responsible for the reducing power in alkaline solution (Smith, *Chem. and Ind.*, 1938, **57**, 450). In support of this theory, it was found that, whereas in aqueous solution no absorption band could be detected, in dilute alkali bands were observed at λ 2790 and λ 4160 A.

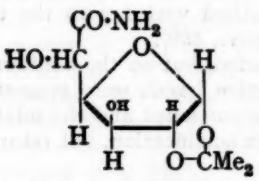
When the crystalline compound (I) was boiled with acid methyl alcohol, there was obtained a liquid dimethyl derivative of glucuronic acid which was non-reducing and behaved as an ester, reacting with one equivalent of alkali and simultaneously losing one methoxyl group. It was shown that the treatment with hot acid methyl alcohol had brought about a ring change from furanose to pyranose and the liquid product was the *methyl* ester of *methylglucopyruronoside* (VII). Methylation with Purdie's reagents yielded the methyl ester of 2 : 3 : 4-trimethyl methylglucuronoside (VIII), which was identified by conversion into the crystalline amide of 2 : 3 : 4-trimethyl α-methylglucuronoside (Smith, J., 1939, 1724).



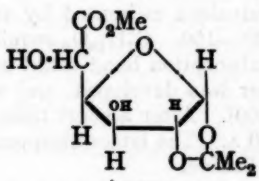
(IX.)



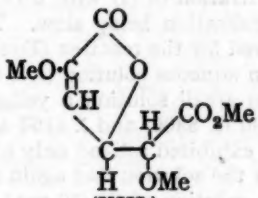
(X.)



(XI.)



(XII.)



(XIII.)

A derivative analogous to (I) with respect to ring form was prepared when glucuronolactone was condensed with acetone in the presence of sulphuric acid, the crystalline product being 1 : 2-*monoacetone glucofururono-γ-lactone* (IX). The furanose structure of this derivative was indicated in that it was possible to prepare it by the lactonisation in a high vacuum of the 1 : 2-monoacetone glucofururonic acid (X) of Zervas and Sessler (*Ber.*, 1933, **66**, 1326). The latter acid is described as a furanose derivative because it is derived from 1 : 2-monoacetone glucofuranose. Additional proof of the structure of (IX) was afforded by the conversion of both the lactone (IX) and the methyl ester (XII) into crystalline 1 : 2-monoacetone glucofururonamide (XI). This amide gave a positive Weerman test for α-hydroxy-amides, indicating the presence of a hydroxyl group at C_5.

In aqueous solution (IX) was neutral to litmus and exhibited no mutarotation; reaction with cold aqueous alkali was slow, and, as in the case of (I), a stoicheiometric relationship was not observed. Furthermore, iodoform was produced by the action of alkaline hypoiodite on (IX) and a reducing action was observed when the compound was added to boiling Fehling's solution. In aqueous solution, no absorption band could be detected but in dilute alkali bands were present at λ 2790 and λ 4100 A.

Methylation of (IX) with Purdie's reagents gave the methyl ester of 2 : 5-dimethyl 2 : 3-dehydrosaccharolactone (XIII) identical with the trimethyl glucuralone described by Pryde and Williams (*Biochem. J.*, 1933, **27**, 1205; compare Pryde and Griffiths, *Chem. and Ind.*, 1938, **57**, 601), the structure of which has been proved by Schmidt, Dippold, and Zeiser (*Ber.*, 1937, **70**, 2402) and by Smith (*Chem. and Ind.*, 1938, **57**, 450). It is evident, therefore, that the unusual properties of (I) and (IX) are due to reactions involving the formation of unsaturated compounds.

Subsequent to the completion of this work in 1939, there has appeared a paper by R. E. Reeves (*J. Amer. Chem. Soc.*, 1940, **62**, 1616), who has demonstrated that the crystalline trimethyl glucurone of Pryde and Williams (*loc. cit.*) has a furanoside and not a pyranoside structure and is, in fact, the γ-lactone of 2 : 5-dimethyl α-methylgluco-

fururonoside. It is claimed that treatment of this substance with methyl-alcoholic hydrogen chloride in the cold brings about its conversion into the isomeric β-form, which should be identical with our product (III). Reeves' substance is, however, crystalline (m. p. 90—91°), whereas ours is a syrup, giving a crystalline amide, m. p. 95°.

Experimental.

γ-Lactone of β-Methylglucofururonoside (I). —Glucuronolactone (1 g.) was dissolved in ½% methyl-alcoholic hydrogen chloride (50 c.c.) and kept at room temperature for 3 days. After neutralisation with silver carbonate, the solution was filtered and evaporated under reduced pressure, and the product recrystallised from alcohol–ether. The *γ-lactone* of *β-methylglucofururonoside* (I) (yield, 0·4 g.) formed colourless prisms, m. p. 139°, $[\alpha]_D^{18°}$ — 57° (*c*, 0·4 in water, unchanged after 48 hours). It was readily soluble in acetone, alcohol, and water, sparingly soluble in ether, and insoluble in light petroleum (Found: C, 44·4; H, 5·5; OMe, 15·5. $C_7H_{10}O_6$ requires C, 44·2; H, 5·3; OMe, 16·3%). On the addition of a small crystal to boiling Fehling's solution, reduction occurred.

The compound (22·12 mg.) in 0·3N-barium hydroxide (3 c.c.) was kept at 60° for 30 minutes. After neutralisation with carbon dioxide and evaporation to dryness, the residue gave silver iodide (18·73 mg.) when an estimation of methoxyl content was carried out. This figure corresponded to OMe 11·2%, calculated on the weight of (I) taken. Slight decomposition had evidently occurred.

Titration of (I) with 0·1N-sodium hydroxide followed the usual course for a γ-lactone, the neutralisation being slow. The equivalent estimated by this method varied with the time allowed for the reaction (Found: 130—150. $C_7H_{10}O_6$ requires equiv., 190).

In aqueous solution (*c*, 0·02) no absorption band could be detected, but on the addition of dilute alkali solution a yellow colour was developed, and absorption bands were present at λ 2790 (ε, 8300) and λ 4160 A. (ε, 8300). After a short time the colour faded and the solution then exhibited a band only at λ 2790 A. The latter disappeared on acidification, but returned when the solution was again made alkaline.

A solution of (I) (50 mg.) in 0·1N-sulphuric acid (50 c.c.) was heated at 90°, the hydrolysis being followed polarimetrically: $[\alpha]_D^{20°}$ — 56° (initial value); — 15° (1 hour); + 19° (3 hours); + 27° (5 hours); + 30° (9 hours). The cooled solution was neutralised with barium carbonate, filtered, treated with a slight deficiency of dilute sulphuric acid, again filtered, and evaporated to dryness under reduced pressure. Extraction of the residue with boiling ethyl acetate gave, after removal of the solvent, crystalline glucuronolactone (28 mg.), m. p. 173° (Found: OMe, nil; equiv. by titration, 171. Calc. for $C_6H_8O_6$: equiv., 176).

The *amide* of *β-methylglucofururonoside* (II) was prepared from (I) (50 mg.) by treatment at 0° with methyl-alcoholic ammonia. The product, a colourless syrup (Found: OMe, 14·7. $C_7H_{13}O_6N$ requires OMe, 15·0%), gave a positive Weerman reaction, hydrazodicarbonamide, m. p. and mixed m. p. 257°, being isolated in good yield.

γ-Lactone of 2 : 5-Dimethyl β-Methylglucofururonoside (III).—(I) (0·2 g.), dissolved in acetone (5 c.c.), was methylated with silver oxide and methyl iodide; the product, which was soluble in methyl iodide, was submitted to two further methylations and then distilled as a colourless syrup (0·14 g.), b. p. (bath temp.) 130—150°/0·01 mm., $n_D^{18°}$ 1·4685 (Found: OMe, 44·6. $C_9H_{14}O_6$ requires OMe, 42·2%). The distillate thus contained a small proportion of a substance of high methoxyl content, probably the methyl ester of 2 : 3 : 5-trimethyl β-methylglucofururonoside. Purification was accomplished by treating the mixture for 20 minutes with a slight excess of cold 0·3N-barium hydroxide, after which any ester present was removed by three extractions with small quantities of chloroform; the *lactone* (III) was then regenerated from the aqueous solution of the barium salt in the usual way. It distilled as a colourless syrup (80 mg.), b. p. (bath temp.) 150°/0·01 mm., $n_D^{18°}$ 1·4732 (Found: OMe, 42·1%). Treatment with methyl-alcoholic ammonia at 0° for 24 hours gave the *amide* of *2 : 5-dimethyl β-methylglucofururonoside* (IV), which crystallised from acetone–ether–light petroleum in plates, m. p. 95° (Found: N, 6·35; OMe, 39·8. $C_9H_{17}O_6N$ requires N, 6·0; OMe, 39·9%).

Formation of 2 : 3 : 5-Trimethyl Saccharolactone Methyl Ester.—The γ-lactone of 2 : 5-dimethyl β-methylglucofururonoside (0·4 g.) (OMe, 44·6%), containing a small quantity of ester (see above), dissolved in water (10 c.c.) and acetone (10 c.c.), was methylated at 40° with methyl sulphate (15 c.c.) and 30% sodium hydroxide solution (40 c.c.), the reagents being added in tenths during 4 hours. The reaction mixture was then heated at 100° for 30 minutes, cooled in ice, acidified with dilute sulphuric acid, and treated with a large excess of alcohol. Sodium

sulphate was removed by filtration, and the solution made faintly alkaline and evaporated to small volume. It was again acidified with sulphuric acid and extracted several times with chloroform. The extracts were washed with a little water, dried over anhydrous magnesium sulphate, filtered, and evaporated to a brown syrup. The crude 2 : 3 : 5-*trimethyl* β-*methylglucuronoside* (V) was acid to litmus and non-reducing to boiling Fehling's solution (Found : OMe, 46·0. $C_{10}H_{18}O_7$ requires OMe, 49·6%). The glycosidic methyl group was removed by heating a solution of the crude material (0·18 g.) in 3% hydrobromic acid at 90° for 8 hours. Bromine (1 c.c.) was then added, and the oxidation allowed to proceed at 50° for 24 hours. The product, isolated in the usual way, was esterified by refluxing for 8 hours with 2% methyl-alcoholic hydrogen chloride (20 c.c.), and yielded a syrup (40 mg.), which crystallised. After two recrystallisations from ether–light petroleum, 2 : 3 : 5-trimethyl saccharolactone methyl ester was obtained in colourless needles, m. p. and mixed m. p. 77—78° (Found : OMe, 50·4. Calc. for $C_{10}H_{16}O_7$: OMe, 50·0%).

Methyl Ester of Methylglucopyruronoside (VII).—A solution of (I) (0·5 g.) in 2% methyl-alcoholic hydrogen chloride (50 c.c.) was refluxed for 6 hours. The cooled solution was neutralised with silver carbonate, filtered, and evaporated under reduced pressure. The *methyl* ester of *methylglucopyruronoside* was obtained as a colourless non-reducing syrup (0·5 g.), $[\alpha]_D^{20°}$ + 88° (*c*, 0·9 in water). It was neutral to litmus and behaved as an ester when warmed with sodium hydroxide solution (Found : OMe, 27·5; equiv. by titration, 224. $C_8H_{14}O_7$ requires OMe, 27·9%; equiv., 222). After treatment for 30 minutes at 60° with 0·3N-barium hydroxide the methoxyl content was 13·3% ($C_8H_{14}O_7$ requires residual OMe, 14·0%).

Formation of the Methyl Ester of 2 : 3 : 4-*Trimethyl Methylglucopyruronoside* (VIII).—The methyl ester of methylglucopyruronoside (0·3 g.) was methylated three times with silver oxide and methyl iodide; the product distilled as a colourless syrup (0·2 g.), b. p. (bath temp.) 120°/0·02 mm., $n_D^{20°}$ 1·4460, $[\alpha]_D^{17°}$ + 84° (*c*, 1·0 in methyl alcohol) (Found : OMe, 57·0; equiv. by titration, 267. Calc. for $C_{11}H_{20}O_7$: OMe, 58·7%; equiv., 264). With methyl-alcoholic ammonia, the ester (27 mg.) was converted into the amide of 2 : 3 : 4-trimethyl α-methyl-glucuronoside, which after recrystallisation from acetone–ether–light petroleum, had m. p. and mixed m. p. 182°.

1 : 2-*Monoacetone Glucofururonolactone* (XII).—(a) *From glucuronolactone.* Glucurono-lactone (1 g.) was dissolved by shaking in dry acetone (50 c.c.) containing concentrated sulphuric acid (0·4 c.c.). The solution was kept for 24 hours, neutralised with barium carbonate, filtered, and evaporated, leaving a solid residue. 1 : 2-*Monoacetone glucofururonolactone* crystallised from ether–light petroleum in colourless needles (0·8 g.), m. p. 120°, $[\alpha]_D^{18°}$ + 70° (*c*, 1·0 in acetone, methyl alcohol and water). It was soluble in water, methyl and ethyl alcohols, acetone, chloroform, ether, and ethyl acetate, insoluble in light petroleum (Found : C, 50·1; H, 5·6. $C_9H_{12}O_6$ requires C, 50·0; H, 5·55%). With aqueous alkali, the substance behaved as a δ-lactone, but estimations of equivalent by titration gave low results [cf. compound (I) above], and with alkaline hypoiodite a precipitate of iodoform was obtained. The compound in aqueous solution (*c*, 0·01) showed no absorption band, but the yellow solution in dilute alkali showed bands at λ 2790 (ε, 7100) and λ 4100 A. (ε, varying with time). On standing, a colourless solution resulted which showed a band only at λ 2790 A.; on acidification this disappeared, but returned when the solution was again made alkaline.

A small quantity of the compound was methylated twice with silver oxide and methyl iodide. The 2 : 5-dimethyl-2 : 3-dehydrosaccharolactone methyl ester (XIII) so obtained, recrystallised first from ether–light petroleum and then from alcohol, had m. p. 89°, $[\alpha]_D$ + 89° and $[\alpha]_{5461}^{17°}$ + 108° (*c*, 1·0 in methyl alcohol) (Found : C, 49·9; H, 5·4; OMe, 42·2. Calc. for $C_9H_{12}O_6$: C, 50·0; H, 5·55; OMe, 43·0%). It gave iodoform on treatment with alkaline hypoiodite and showed an absorption band at λ 2290 A. (ε, 6546) which moved to λ 3010 A. (ε, 3240) when the solution was made alkaline.

(b) *From* 1 : 2-*monoacetone glucofururonic acid.* The acid (X) (30 mg.), prepared by the method of Zervas and Sessler (*loc. cit.*), was heated at 95—100°/0·01 mm. for an hour. On the cooler portion of the vessel was formed a crystalline sublimate, m. p. 119°, not depressed on admixture with (IX) prepared from glucuronolactone. A mixed m. p. with the original acid (X) (m. p. 146°) was 108—110°.

1 : 2-*Monoacetone Glucofururonamide* (XI).—(a) *From* 1 : 2-*monoacetone glucofururono-lactone.* The compound (0·1 g.) was dissolved in dry methyl alcohol (5 c.c.) saturated with dry ammonia at 0°, and kept at this temperature for 24 hours. Thereafter the solvent was removed by evaporation in a vacuum and the solid residue was recrystallised from alcohol–ether. 1 : 2-*Monoacetoneglucofururonamide* formed colourless prisms, m. p. 164° (decomp.),

$[\alpha]_D^{18°}$ — 14° (*c*, 0·9 in water) (Found: C, 46·5; H, 6·3; N, 6·2. $C_9H_{15}O_6N$ requires C, 46·4; H, 6·5; N, 6·0%).

A solution of the amide (30 mg.) in water (1 c.c.) was treated with a slight excess of 1·5N-sodium hypochlorite for 30 minutes at 0°; the excess was then removed by the addition of a few drops of sodium thiosulphate solution. On the addition of sodium acetate, followed by semicarbazide hydrochloride, a precipitate of hydrazodicarbonamide was obtained, m. p. and mixed m. p. 258°.

(b) *From* 1 : 2-*monoacetone glucofururonic acid.* The acid (30 mg.), suspended in dry ether (3 c.c.), was treated with a slight excess of an ethereal solution of diazomethane. The liquid ester obtained on evaporation was treated with methyl-alcoholic ammonia at 0° for 36 hours. Removal of the solvent gave a solid residue, which, after recrystallisation from alcohol–ether, had m. p. (with decomposition) 164°, unchanged on admixture with (XI) obtained from 1 : 2-monoacetone glucofururonolactone.

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66. *Studies in the Sterol Group. Part XLIII. The Unsaponifiable Portion of the Acetone Extract of Plantation Rubber.*

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In previous studies of this material the isolation and identification of a sterol, $C_{27}H_{46}O$ (Whitby, Dolid, and Yorston, J., 1926, 1448), and octadecyl alcohol (Bruson, Sebrell, and Vogt, *Ind. Eng. Chem.*, 1927, **19**, 1187) have been described. It is now shown that the former is a mixture of isomeric sterols which includes β-sitosterol and probably a 24 : 28-dehydrostigmastanol, and that the aliphatic alcohol is eicosyl alcohol. No other pure constituent has as yet been isolated in sufficient quantity for investigation, since the remainder of the neutral fraction undergoes extensive pyrolysis on distillation even in a high vacuum. Evidence has, however, been obtained that a portion of the unsaponifiable matter becomes increasingly intractable as rubber ages, and it is possible that the present failure to obtain the ketone $C_{15}H_{24}O$ and the so-called "liquid sterols," $C_{27}H_{42}O_3$ and $C_{20}H_{30}O$, reported by Bruson, Sebrell, and Vogt (*loc. cit.*) may be due to this cause.

THE raw material of the present investigation was the acetone extract of 100 lb. of plantation crepe rubber. On concentration, this deposited a few grams of sparingly soluble material consisting of quebrachitol, sterol glucoside, and nitrogenous and phosphatic matter. The unsaponifiable portion, isolated by the usual methods, yielded on treatment with alcohol a crystalline solid and a mother-liquor from which a reddish gum was obtained.

The solid fraction, after repeated crystallisation, had m. p. 135·5° (Whitby, Dolid, and Yorston, *loc. cit.*, give m. p.'s 133—134°, 134—135°, and 125° for various preparations), and was characterised readily by the preparation of acetyl, benzoyl, and *p*-nitrobenzoyl derivatives. Analytical evidence suggested the composition $C_{29}H_{50}O$; this was confirmed by quantitative hydrolysis of the acetate and by a molecular-weight determination based on *X*-ray data, for which we are indebted to Miss D. Crowfoot. Titration with perbenzoic acid indicated the presence in the molecule of one double bond, and the isolation of a substance indistinguishable from stigmastanyl acetate on catalytic hydrogenation of the acetate revealed that the material belonged to the phytosterol group. Further evidence of this association was forthcoming from a selenium dehydrogenation carried out at a high temperature, hydrocarbons similar to those obtained from sterols under like conditions (Ruzicka, Thomann, Brandenburger, and Goldberg, *Helv. Chim. Acta*, 1934, **17**, 200; Ruzicka, Goldberg, and Thomann, *ibid.*, 1933, **16**, 812) being obtained. These included a *chrysene*, m. p. 172—173°, and a *picene*, m. p. 274—276°, their respective struc-

tures being deduced from their absorption spectra, which are closely analogous to those described by Mayneord and Roe (*Proc. Roy. Soc.*, 1935, *A*, **152**, 319) for chrysene and picene. In addition there was isolated a ***hydrocarbon***, m. p. 227° (2 : 7-dinitroanthraquinone derivative, m. p. 242—243°), which, although quite similar to, is not identical with either of the hydrocarbons obtained by Ruzicka *et al.* (*loc. cit.*) from phytosterols.

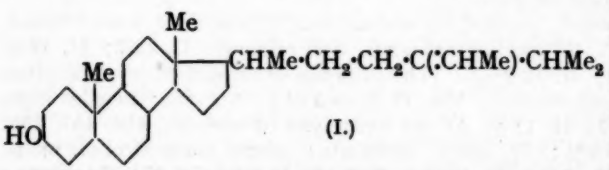
Despite the apparent homogeneity of the sterol as outlined above, chromatographic analysis demonstrated that it was actually a mixture, although a pure component could not be obtained by this means. This was also suggested by *X*-ray diffraction photographs, which showed a very close relationship with certain phytosterol mixtures (private communication from Miss D. Crowfoot). A more effective resolution was obtained by repeated fractional crystallisation of the acetate, which resulted in the separation of two distinct components. For convenience the corresponding sterols will be referred to as sterols A and B, and their physical constants, together with those of the corresponding acetyl and benzoyl derivatives, are summarised in the accompanying table with similar data for β-sitosterol (Wallis and Chakravorty, *J. Org. Chem.*, 1937, **2**, 335; see also Heilbron and Jones, *Ann. Rev. Biochem.*, 1940, **9**, 163) :

	Sterol.		Acetyl derivative.		Benzoyl derivative.	
	M. p.	$[\alpha]_D^{20°}$.	M. p.	$[\alpha]_D^{20°}$.	M. p.	$[\alpha]_D^{20°}$.
β-Sitosterol	136—137°	−37°	125—126°	−41°	146—147°	−13·8°
Sterol A	135·5	−37	123·5	−41	147	−15·2
Sterol B	134	−26	114—116	−28	145	−14·9

The results recorded above indicate that sterol A is identical with β-sitosterol and no depression in melting point was observed on admixture with authentic material from wheat germ oil. Further, catalytic hydrogenation of sterol A gave stigmastanol indistinguishable from specimens obtained by the authors by the complete hydrogenation of fucosterol (cf. Coffey, Heilbron, and Spring, J., 1936, 738).

	Alcohol.		Acetyl derivative.		Phenylurethane.	
	M. p.	$[\alpha]_D^{20°}$.	M. p.	$[\alpha]_D^{20°}$.	M. p.	$[\alpha]_D^{20°}$.
Stigmastanol	133°	+23°	128·5—129·5°	+13·0°	169—170°	+13·8°
Dihydro-sterol A	133—133·5	+23	128—128·5	+11·5	169—170	+13·9
Dihydro-sterol B	126·5	+ 5·8	122—123	− 8·2		

Sterol B, composing rather less than 10% of the original sterol mixture, on titration with perbenzoic acid gave a value corresponding to one ethenoid linkage, and on ozonolysis of the acetate, acetaldehyde was obtained in 22% yield (estimated as the 2 : 4-dinitrophenylhydrazone), indicating the presence of an ethylidene group in the side chain and suggesting the constitution (I) for this sterol. Only a trace of formaldehyde and no acetaldehyde could be detected on ozonolysis of the hydrogenation product of the acetyl derivative of sterol B. The latter is not, however, identical with stigmastanyl acetate (see table), a fact which is not entirely unexpected, since reduction of the ethenoid linkage involves the introduction of an asymmetric centre at C_{24}. In this connection it might be noted that campesterol (Fernholz and Ruigh, *J. Amer. Chem. Soc.*, 1941, **63**, 1157) differs from 22 : 23-dihydrobrassicasterol only in the optical configuration about C_{24}. We would emphasise that sterol B has not yet been obtained completely free from β-sitosterol, since a small quantity of an αβ-unsaturated ketone was isolated from the product of oxidation by the Oppenauer method. Limited by the availability of material, attempts to isolate in a pure condition the 24 : 28-dehydrostigmastanol (I), which is almost certainly the major constituent of the sterol B complex, have been unsuccessful and, as it is impossible meantime to continue this work, it has been decided to place the results on record. It has recently been demonstrated that the unsaturated side chains of brassicasterol (Fernholz and Stavely, *J. Amer. Chem. Soc.*, 1940, **62**, 1875) and α-spinasterol (Fernholz and Ruigh, *ibid.*, p. 2341) are identical with those of ergosterol and stigmasterol respectively and that the side chain of zymosterol



(I.)

contains an *iso*propylidene group (Heath-Brown, Heilbron, and Jones, J., 1940, 1482). The suggestion that the non-saponifiable portion of the acetone extract of rubber contains a sterol in which an ethylidene group is located in the side chain is of interest in that it points to the existence of yet another type of unsaturated side chain in naturally occurring sterols.

When the reddish gum from the original mother-liquor was distilled in a high vacuum (10^{-3} mm.), a colourless waxy substance passed over at 80—90°. This was readily purified and its constants together with those of the acetyl derivative and *phenylurethane* prove it to be eicosyl alcohol and not octadecyl alcohol, as suggested by Bruson, Sebrell, and Vogt (*loc. cit.*), who actually call attention to the fact that their "octadecyl alcohol" depressed slightly the melting point of an authentic specimen. The crystalline distillate obtained at 120—130° is probably steroid in nature. Above this temperature extensive decomposition occurred, and the small quantity of viscous oil which distilled contained ketonic material, part of which was identified by the preparation of a 2 : 4-dinitrophenylhydrazone giving the analysis required for the derivative of a steroid ketone. The remainder of the ketonic fraction yielded a complex dinitrophenylhydrazone which could not be resolved; that this is a product of pyrolytic decomposition was revealed by the fact that treatment of the original gum with the Girard reagent P failed to reveal the presence of any ketonic matter. Since high-vacuum distillation yielded no satisfactory separation, attention was directed to the removal of hydroxylic compounds from the original gum by means of the acid succinates, but this only resulted in the isolation of a further quantity of the sterol mixture and eicosyl alcohol. Careful fractionation of the non-hydroxylic residue both by distillation in a high vacuum and by solvent treatment failed to yield any tractable material. Examination of the acetone extract of crepe rubber twelve months older than that employed in the above investigation revealed an even lower proportion of volatile non-hydroxylic matter.

Experimental.

All rotations were carried out in chloroform solution in a 1 dcm. tube. Melting points are uncorrected.

The crude acetone extract from crepe rubber (100 lb.), concentrated to 2·5 l., was filtered and evaporated to dryness under reduced pressure. The residue (1100 g.) was shaken for 72 hours with methyl-alcoholic potassium hydroxide (5 l.; 5%), the alcohol removed under reduced pressure, and the residue extracted with ether. Washing the extract with water yielded a deep red, voluminous aqueous phase and a yellow ethereal phase which contained the bulk of the unsaponifiable matter. A considerable further quantity of the latter, however, was obtained by re-extracting the aqueous phase with much ether. The total unsaponifiable fraction (210 g.) in hot alcohol (4 l.) was decanted from a small amount of tarry matter and cooled; the crude sterol (85 g.) then separated. Removal of solvent from the mother-liquor under diminished pressure yielded an oily red gum.

The Sterol Mixture.—The crude sterol, purified by several recrystallisations from alcohol, formed colourless plates, m. p. 133·5°. $\overset{=}{|}$ (perbenzoic acid), 0·97 (Found : C, 82·7; H, 12·0. Calc. for $C_{29}H_{50}O,\frac{1}{2}C_2H_5{\cdot}OH$: C, 82·3; H, 12·2%). (The presence of alcohol of crystallisation is confirmed by the *X*-ray investigations made by Miss D. Crowfoot.) Acetate : needles from alcohol, m. p. 123·5° [Found : C, 81·7; H, 11·5; *M* (by hydrolysis of acetate), 456, 457, 455. Calc. for $C_{31}H_{52}O_2$: C, 81·5; H, 11·6%; *M*, 456]. Benzoate : plates from alcohol, m. p. 147·5° (Found : C, 83·4; H, 10·6. Calc. for $C_{36}H_{54}O_2$: C, 83·3; H, 10·5%). *p*-Nitrobenzoate : pale yellow micro-needles from alcohol, m. p. 183—184° (Found : C, 76·8; H, 9·6. Calc. for $C_{36}H_{53}O_4N$: C, 76·7; H, 9·5%). Dihydro-derivative of acetate (by reduction of acetate in the presence of Adams's catalyst at room temperature and pressure) : plates from acetone, m. p. 130·5°, $[\alpha]_D^{20°}$ + 14·3° (*c*, 2·0) (Found : C, 81·4; H, 11·7. Calc. for $C_{31}H_{54}O_2$: C, 81·1; H, 11·9%). The dihydro-sterol obtained by alkaline hydrolysis of the dihydro-acetate formed plates from acetone, m. p. 134·5—135·5°, $[\alpha]_D^{20°}$ + 24° (*c*, 1·8), and gave a slight Liebermann–Burchard test (Found : C, 83·7; H, 12·7. Calc. for $C_{29}H_{52}O$: C, 83·6; H, 12·6%).

Selenium Dehydrogenation of the Sterol Mixture.—The dry mixed sterol (35 g.) was heated with dry selenium (60 g.) in a nitrite bath, the temperature of which varied between 320° and 400° during 72 hours. The pulverised product was extracted (Soxhlet) first with ether and then with benzene. Traces of phenolic substances were removed on washing the diluted ethereal extract with alkali; it was subsequently washed with water, dried, and evaporated, and the residue adsorbed from benzene solution on alumina. Elution of the chromatogram with

benzene gave a pale yellow, green-fluorescent solution and the subsequent ethereal washings were added to the original benzene extract. The solid product obtained on evaporation of the benzene eluate on trituration with cold ether gave a pale yellow substance, which after an elaborate purification yielded an almost colourless *picene* derivative, m. p. 274—276° (Found: C, 93·8; H, 6·15. $C_{28}H_{20}$ requires C, 93·7: H, 6·3%).

The original benzene extract, together with the ethereal eluate from the chromatogram, was evaporated and a benzene solution of the residue was adsorbed on alumina. The solid (3·1 g.) from the first 2500 c.c. of eluate was taken up in light petroleum (b. p. 40—60°)–benzene (1 : 1) and refractionated through alumina. The initial and the final runnings, which contained waxy and gummy matter respectively, were neglected; two of the remaining fractions, after elaborate processes involving washing, crystallisation, sublimation, and readsorption on alumina, ultimately yielded two substances. (a) A *chrysene* derivative, m. p. 172—173° [Found: C, 93·6; H, 6·5; *M* (Rast), 279. $C_{21}H_{18}$ requires C, 93·3; H, 6·7%; *M*, 270]. (b) A *hydrocarbon*, m. p. 227° (Found: C, 92·6; H, 7·4. $C_{25}H_{24}$ requires C, 92·5; H, 7·4%), giving a 2 : 7-dinitroanthraquinone derivative, m. p. 242—243°.

Resolution of the Sterol Mixture.—The sterol mixture (950 mg.) was refluxed for 1 hour with acetic anhydride (10 c.c.) and pyridine (10 c.c.). The product, isolated by pouring into water, yielded two acetates on fractional crystallisation: A (600 mg.), m. p. 123·5°, $[\alpha]_D^{20°}$ − 41° (*c*, 2·3), and B (50 mg.), m. p. 114—116°, $[\alpha]_D^{20°}$ − 28° (*c*, 1·5). A mixture of these two acetates in approximately equal amounts had m. p. 116—119°.

Sterol A (β-*Sitosterol*).—Hydrolysis of acetate A with methyl-alcoholic potassium hydroxide (5%) yielded sterol A, which formed plates from methyl alcohol–acetone, m. p. 135—135·5°, $[\alpha]_D^{20°}$ − 37° (*c*, 1·6). $\dagger$ (perbenzoic acid), 1·09. Benzoate: m. p. 147°, $[\alpha]_D^{20°}$ − 15·2° (*c*, 2·6). Reduction of acetate A in acetic acid with hydrogen and Adams's catalyst at room temperature and pressure yielded the corresponding dihydro-acetate, which formed plates from methyl alcohol–acetone, m. p. 128—128·5°, $[\alpha]_D^{20°}$ + 11·5° (*c*, 1·8). This on alkaline hydrolysis was converted into the dihydro-sterol, m. p. 133—133·5°, $[\alpha]_D^{20°}$ + 23° (*c*, 2·5). Phenylurethane: m. p. 169—170°, $[\alpha]_D^{20°}$ + 13·9° (*c*, 1·6).

Sterol B.—The acetate B similarly gave sterol B in plates, m. p. 134°, $[\alpha]_D^{20°}$ − 26° (*c*, 2·1). $\dagger$ (perbenzoic acid), 1·02. Benzoate: m. p. 145°, $[\alpha]_D^{20°}$ − 14·9° (*c*, 2·0). Reduction of acetate B under the above conditions gave a crystalline product, m. p. 122—123°, $[\alpha]_D^{20°}$ − 8·2° (*c*, 2·0), which, after alkaline hydrolysis, had m. p. 126·5—127°, $[\alpha]_D^{20°}$ + 5·8° (*c*, 1·2).

Ozonolysis of acetate B gave a volatile aldehyde, which was converted into the 2 : 4-dinitrophenylhydrazone. This, after purification through alumina and crystallisation from alcohol, had m. p. 158—159°, undepressed by authentic acetaldehyde-2 : 4-dinitrophenylhydrazone (yield, 22%) (Found: N, 25·1. Calc. for $C_8H_8O_4N_4$: N, 25·0%). Ozonolysis of the dihydro-acetate described above gave no acetaldehyde.

Sterol B on oxidation with aluminium *tert.*-butoxide and acetone in the usual manner produced in small yield a ketone, m. p. 92—95°. Light absorption in alcohol: Max. 2410 A.; $\log \varepsilon = 3·9$.

The Red Gum.—This material, when heated in a retort at 80—90/10^{-3} mm., gave a waxy distillate of eicosyl alcohol, which crystallised from methyl alcohol in leaflets, m. p. 62° (Adam and Dyer, J., 1925, **127**, 70, give m. p. 65·0—65·5°). Acetate: needles, m. p. 41° (lit., 39·5—40·5°). *Phenylurethane:* plates from methyl alcohol, m. p. 75—76° (Found: C, 77·8; H, 11·3. $C_{27}H_{47}O_2N$ requires C, 77·6; H, 11·3%). At 110—130° some crude sterol sublimed from the gum and at 140—150° a pale yellow, viscous oil with ketonic properties distilled slowly. Volatile products of decomposition were also evident, and the viscid residue in the retort had darkened in colour and become insoluble in acetone. The distillate obtained at 140—150° was treated with 2 : 4-dinitrophenylhydrazine hydrochloride in alcohol and the resulting red solid, dissolved in benzene, was towered on alumina. The benzene washings were evaporated, and the residue crystallised fron benzene–methyl alcohol, giving scarlet prisms, m. p. 239—240° (Found: C, 70·9; H, 8·8. $C_{35}H_{52}O_4N_4$ requires C, 70·9; H, 8·8%). The mother-liquor from the crystallisation of the above substance contained a second 2 : 4-dinitrophenylhydrazone, which crystallised from light petroleum (b. p. 60—80°) in golden leaflets, m. p. 121—123°, but the analytical data for this material could not be interpreted.

The above work has been carried out as part of the programme of fundamental research on rubber undertaken by the Board of the British Rubber Producers' Research Association.

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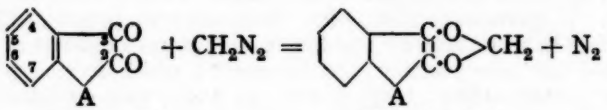
67. *The Formation of Methylene Ethers by the Action of Diazomethane* on α-Keto-lactones and on Diphenyl Triketone, with a Note on the Pyrolysis of Coumarandione and Allied Substances.*

By Alexander Schönberg, Radwan Moubasher, and (in part) (Miss) Akila Mostafa.

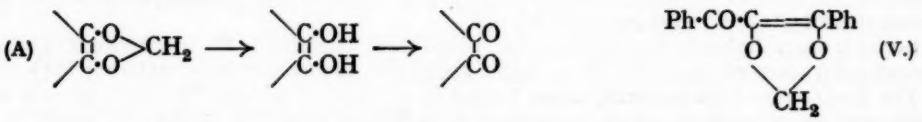
The *methylene* ether (III) was obtained by the action of diazomethane on coumarandione (I). Similar reactions took place with its derivatives and with diphenyl triketone [formation of (V)]. Coumarandione, thiocoumarandione (II) and allied substances are thermolabile; at 200° they furnish xanthone and its derivatives respectively.

(A) Ring expansion occurs with the formation of a quinoline derivative when *N*-methylisatin acts upon diazomethane (Heller, *Ber.*, 1926, **59**, 704). From coumarandione (I) and thiocoumarandione (II) (thionaphthenquinone), which may be regarded as analogues of *N*-methylisatin, and also from 4 : 5- and 6 : 7-benzocoumaran-2 : 3-dione, by reaction with diazomethane, we have obtained *methylene* ethers. Unlike the parent compounds, the ethers (III), (IV), and (VI) are colourless, because they no longer contain the chromophor



(I, A = O.) (II, A = S.) (III, A = O.) (IV, A = S.)

CO·CO. They may be regarded as acetals and, as such, are acted upon by acids. The products, when heated, undergo aerial oxidation and furnish coumarandione (I), thiocoumarandione (II), and 4 : 5-benzocoumaran-2 : 3-dione respectively, the ready formation of which (illustrated by scheme A) excludes the formation of an ethylene oxide ring by the action of diazomethane on coumarandione and its derivatives (compare Arndt, Amende, and Ender, *Monatsh.*, 1932, **59**, 202).



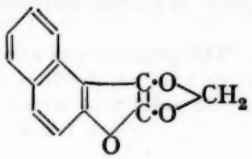
So far as we are aware, the formation of methylene ethers by the action of diazomethane on keto-lactones (to which class of substances the coumarandiones belong) has not previously been observed. The reaction is well known with 1 : 2-diketones and *o*-quinones, *e.g.*, benzil and phenanthraquinone (Arndt, Amende, and Ender, *loc. cit.*). Diphenyl triketone reacts according to our observation in a similar way with the formation of αβ-*methylenedioxy-β-benzoyl-α-phenylethylene* (V). After treatment with hydrochloric acid, the product, on aerial oxidation, furnished diphenyl triketone hydrate (cf. Scheme A).

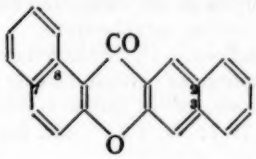
(B) Continuing the researches of the senior author on the pyrolysis of organic compounds and the relation between constitution and thermolability (for earlier papers on this subject by A. Schönberg and co-workers, see J., 1935, 1403, footnote; *Ber.*, 1938, **71**, 995; J., 1939, 1431), we have investigated coumarandione (I) and some of its derivatives.

At 200°, coumarandione (I) and thiocoumarandione (II) yield xanthone and thioxanthone respectively, and 4 : 5-benzocoumaran-2 : 3-dione furnishes a mixture from which 2 : 3 : 7 : 8-

* For earlier papers by A. Schönberg and co-workers on the action of diazomethane and its derivatives on organic substances without active hydrogen atoms, see *Ber.*, 1929, **62**, 440, 1663; 1930, **63**, 3102; 1931, **64**, 1390, 2324, 2577; 1932, **65**, 289; 1933, **66**, 246; *Annalen*, 1930, **483**, 176.

dibenzoxanthone (VII) has been obtained. Fries and Pfaffendorf (*Ber.*, 1912, **45**, 156) obtained a compound, $(C_7H_4O_2)_x$, on heating coumarandione at 220° under ordinary

(VI.) 

 (VII.)

conditions, whereas our above-mentioned experiments were carried out in an atmosphere of carbon dioxide.

Experimental.

(A) The reactions with diazomethane were all carried out in the way described below.

With Coumarandione.—To an ethereal solution of excess of diazomethane (Arndt and Amende, *Z. angew. Chem.*, 1930, **45**, 444), coumarandione (I) (Fries and Pfaffendorf, *Ber.*, 1912, **45**, 154) (1 g.) was added at a low temperature. Evolution of nitrogen took place and the solution was left in the ice-chest for 24 hours. The solvent was driven off in a vacuum, and the residue dried over phosphoric oxide and crystallised several times from benzene (charcoal). **2 : 3-*Methylenedioxycoumarone*** (III) tended to form an oil, but was obtained in colourless needles easily soluble in benzene, alcohol, and acetic acid; it had m. p. 110°, forming a yellowish-red melt [Found: C, 67·1; H, 3·5; *M* (in camphor), 154. $C_9H_6O_3$ requires C, 66·7; H, 3·7%; *M*, 162].

The ether (1 g.) was refluxed for 6 hours with 30 c.c. of hydrochloric acid (*d* 1·16). Cold water was added to the cold product. The colourless precipitate obtained became yellow during filtration; it was dried on a porous plate to complete the oxidation to coumarandione (I), which, after recrystallisation from benzene, had m. p. 134°, undepressed by an authentic specimen.

With Thiocoumarandione (II) * (Pummerer, *Ber.*, 1910, **43**, 1372).—The crude reaction product was dissolved in dry benzene and treated with charcoal; thus purified, it was dried over phosphoric oxide and crystallised from benzene. **2 : 3-*Methylenedioxythionaphthen*** (IV) was obtained in colourless needles, easily soluble in benzene and alcohol; it had m. p. 130°, giving a brown liquid (Found: C, 60·4; H, 3·2; S, 17·8. $C_9H_6O_2S$ requires C, 60·5; H, 3·3; S, 17·9%).

On hydrolysis of the ether and oxidation of the product as described above, thiocoumarandione was obtained, m. p. and mixed m. p. 120°.

With **4 : 5-*Benzocoumaran*-2 : 3-*dione*** (Giua and Franciscis, *Gazzetta*, 1924, **54**, 509).—The product was purified as in the preceding case. **2 : 3-*Methylenedioxy*-4 : 5-*benzocoumarone*** (VI) was obtained in colourless needles, m. p. 189—190°, easily soluble in benzene, alcohol, and acetic acid (Found: C, 73·5; H, 4·3. $C_{13}H_8O_3$ requires C, 73·5; H, 3·8%).

Hydrolysis of the ether, followed by aerial oxidation, gave **4 : 5-benzocoumaran-2 : 3-dione**, m. p. (after crystallisation from benzene) and mixed m. p. 182°.

With **6 : 7-*Benzocoumaran*-2 : 3-*dione*** (Giua and Franciscis, *loc. cit.*).—The product, **2 : 3-*methylenedioxy*-6 : 7-*benzocoumarone***, after purification, was obtained in colourless needles easily soluble in benzene and alcohol; it had m. p. 155° with formation of a red-brown liquid (Found: C, 73·3; H, 3·8. $C_{13}H_8O_3$ requires C, 73·5; H, 3·8%).

Hydrolysis of the ether and aerial oxidation furnished **6 : 7-benzocoumaran-2 : 3-dione**, m. p. and mixed m. p. 146°.

With Diphenyl Triketone.—After distillation of the ethereal solvent the oily residue was treated with benzene (distilled over sodium) and charcoal for 6 hours. The almost colourless filtrate, on addition of light petroleum (b. p. 60—70°), deposited ***αβ-methylenedioxy-β-benzoyl-α-phenylethylene*** (V), which, recrystallised from alcohol (2 vols.) and water (1 vol.), formed colourless needles, m. p. 160° (yield, 0·2 g. from 1 g. of the triketone) (Found: C, 76·0; H, 5·4. $C_{16}H_{12}O_3$ requires C, 76·2; H, 4·7%).

The ethylene derivative (V) was refluxed with concentrated hydrochloric acid for 12 hours, and the product cooled and poured into ice-water. The solid formed was dried and dissolved in boiling benzene, and oxygen passed through the solution. After 2 hours the benzene was driven off, and the residue crystallised from dilute acetic acid, giving colourless crystals

* This experiment and the pyrolysis of thiocoumarandione were performed by Miss Akila Mostafa.

which proved by their m. p. and their mixed m. p. with an authentic specimen to be diphenyl triketone hydrate.

(B) Pyrolysis in all cases was carried out in an atmosphere of carbon dioxide in a vessel immersed in boiling nitrobenzene.

Coumarandione.—Pyrolysis was carried out for 6 hours. The product was allowed to cool in the atmosphere of carbon dioxide and was then sublimed in a vacuum (bath at about 190°), giving xanthone, m. p. (after crystallisation from glacial acetic acid) and mixed m. p. 174° (Found : C, 79·7; H, 4·2. Calc. for $C_{13}H_8O_2$: C, 79·6; H, 4·1%). Yield, 0·4 g. from 1 g. of the dione.

In a similar way thiocoumarandione gave thioxanthone, which crystallised from benzene in needles, m. p. 207°, undepressed by an authentic specimen.

4 : 5-*Benzocoumaran*-2 : 3-*dione.*—Pyrolysis (1 hour) and cooling were carried out as in the case of coumarandione. The product was boiled with a small quantity of benzene to remove unchanged substance. The yellow residue was dissolved in a large quantity of boiling benzene, cooled, and precipitated with light petroleum (b. p. 60—70°). The amorphous substance thus obtained was sublimed in a vacuum, giving yellowish crystals of 2 : 3 : 6 : 7-dibenzoxanthone (VII) (Dilthey and Stephan, *J. pr. Chem.*, **1939**, **152**, 119), m. p. 238° after recrystallisation from glacial acetic acid (2 vols.)–95% ethyl alcohol (1 vol.).

FOUAD I UNIVERSITY, CAIRO. [*Received, April 24th,* 1941.]

NOTES.

p-*Aldehydophenyltrimethylammonium Salts and their Condensation and Decomposition Products.*

By AHMAD ZAKI and WADIE TADROS.

p-*Aldehydophenyltrimethylammonium Salts.*—The *picrate* was precipitated in golden-yellow plates or feathery crystals when aqueous solutions of picric acid and of the dark red product obtained from the interaction of methyl sulphate and *p*-dimethylaminobenzaldehyde (Zaki, J., 1930, 1078. It is not necessary to isolate the *p*-aldehydophenyltrimethylammonium methosulphate) were mixed. Recrystallised twice from hot water (charcoal), the picrate had m. p. 169°. Yield, 50% (Found : C, 48·9; H, 4·0; N, 13·8. $C_{16}H_{16}O_8N_4$ requires C, 49·0; H, 4·1; N, 14·3%).

Chloride. The picrate was warmed with concentrated hydrochloric acid. After cooling, the precipitated picric acid was removed, the filtrate washed with ether or benzene and evaporated to dryness, and the residue crystallised from absolute alcohol, the *chloride* separating in colourless crystals, m. p. 191°, readily soluble in water and warm 96% ethyl alcohol, insoluble in ether, benzene, and acetone (Found : C, 60·1; H, 7·1; N, 7·1; Cl, 17·8. $C_{10}H_{14}ONCl$ requires C, 60·1; H, 7·1; N, 7·0; Cl, 17·8%). Addition of ether to the alcoholic mother-liquor precipitated a second crop of the chloride.

Iodide. (a) A mixture of *p*-dimethylaminobenzaldehyde (10 g.) and excess of methyl iodide (50 g.) was refluxed for 15—20 hours, and the excess then recovered by distillation. When the residue was washed with ether, the *iodide* was obtained in colourless crystals. (b) When saturated aqueous solutions of the above chloride and potassium iodide were mixed, the iodide separated in colourless crystals, m. p. 164—165°, soluble in water and hot alcohol, insoluble in ether, benzene, and acetone (Found : I, 43·1. $C_{10}H_{14}ONI$ requires I, 43·6%).

The perchlorate, precipitated on addition of a few c.c. of 30% perchloric acid solution to a concentrated aqueous solution of the chloride, crystallised from water in colourless plates, m. p. 143° (Found : Cl, 13·4. Calc. for $C_{10}H_{14}O_5NCl$: Cl, 13·5%).

Chloride perbromide. Solutions of a slight excess of bromine (3·5 g.) and the chloride (3 g.) in acetic acid (10 c.c. each) were mixed and left overnight in the ice-chest. The precipitated perbromide separated from acetic acid in orange-red crystals, m. p. 115—116°. It was unstable and the colour disappeared entirely within 8—10 weeks.

Condensation Products.—(1) A mixture of the iodide (1 g.), hydroxylamine hydrochloride (1·2 g., dissolved in the least quantity of water), sodium carbonate (1 g.), and absolute alcohol (10 c.c.) was refluxed for 3 hours, and the alcohol then distilled off from the filtered solution. To an aqueous solution of the residue aqueous picric acid was added, precipitating the *picrate* of the *oxime*, which crystallised from water in yellow needles, m. p. 201—202° (Found : C, 47·6; H, 4·5; N, 17·4. $C_{16}H_{17}O_8N_5$ requires C, 47·2; H, 4·3; N, 17·2%).

(2) The *picrate* of the *semicarbazone*, obtained in the same way (iodide, 2 g.; semicarbazide hydrochloride, 0·9 g.; sodium acetate, 0·6 g.; absolute alcohol, 10 c.c.), separated from water in orange-yellow crystals, m. p. 227—228° (Found: C, 45·6; H, 4·3; N, 21·7. $C_{17}H_{19}O_8N_7$ requires C, 45·4; H, 4·2; N, 21·8%).

(3) The *picrate* of the *phenylhydrazone*, also obtained similarly (iodide, 1 g.; phenylhydrazine hydrochloride, 0·7 g.; sodium acetate, 0·5 g.; absolute alcohol, 20 c.c.), crystallised from dilute alcohol in orange-yellow needles, m. p. 200—201°, very sparingly soluble in water (Found: C, 54·2; H, 4·5; N, 17·5. $C_{23}H_{23}O_7N_6$ requires C, 54·8; H, 4·6; N, 17·4%).

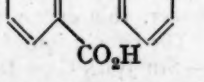
(4) A mixture of the chloride (3 g.) and *m*-nitroaniline (3 g.) was heated at 160—165° for an hour. The product was dissolved in water, and picric acid added to the filtered solution. The voluminous *picrate* of the condensation product crystallised from dilute alcohol in reddish-brown needles, m. p. 208° (Found: C, 50·7; H, 4·1; N, 16·8. $C_{23}H_{20}O_9N_6$ requires C, 51·4; H, 3·9; N, 16·4%).

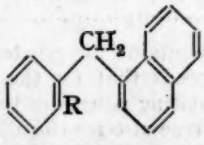
Decomposition of the Chloride.—A mixture of the chloride (2 g.) and alcoholic sodium ethoxide (0·5 g. of sodium in 40 c.c. of absolute alcohol) was refluxed for 3 hours. After dilution with water, the solution was extracted with ether. The extract contained two components: (*a*) *p*-dimethylaminobenzaldehyde (0·48 g.), m. p. and mixed m. p. 73°, separated by shaking with dilute hydrochloric acid; (*b*) *p*-ethoxybenzaldehyde (0·75 g.), obtained as a brownish oily residue after evaporation of the ether. [The influence of the aldehydo-group in producing the latter type of fission is shown by comparison with the decomposition of phenyltrimethylammonium and phenylbenzyldimethylammonium chlorides by alcoholic sodium ethoxide (Vorländer and Spreckels, *Ber.*, 1919, **52**, 309); in both these cases one route is followed, yielding dimethylaniline.] The latter was oxidised by alkaline potassium permanganate to *p*-ethoxybenzoic acid, m. p. 195° (Gattermann, *Annalen*, 1907, **357**, 348). The alkaline solution was freed from ether by warming and just acidified with acetic acid; a trace of *p*-dimethylaminobenzoic acid, m. p. and mixed m. p. 233°, was the only precipitate.—FOUAD I UNIVERSITY, CAIRO, EGYPT. [*Received, May 5th*, 1941.]

Derivatives of o-1-*Naphthoylbenzoic Acid and* 1-*Benzylnaphthalene-2′-carboxylic Acid.*

By G. M. BADGER.

IN connection with a scheme, now indefinitely postponed, for the synthesis of certain complex fluorene derivatives, the Curtius degradation has been attempted with *o*-1-naphthoylbenzoic acid (I). The ethyl ester of this acid reacted with hydrazine hydrate to form 4-*keto*-1-(1′-*naphthyl*)-3 : 4-*dihydrophthalazine*. However, the reduced acid, 1-benzylnaphthalene-2′-carboxylic acid (II, R = CO_2H), was successfully degraded to 1-o-*aminobenzylnaphthalene*.

(I.) 



(II.)

Ethyl *o*-1-naphthoylbenzoate, prepared from the acid (2 g.) by 7 hours' boiling with alcohol (50 c.c.) and sulphuric acid (1 c.c.), formed colourless transparent prisms, m. p. 81·5—83° (Found: C, 78·65; H, 5·4. Calc. for $C_{20}H_{16}O_3$: C, 78·9; H, 5·3%). Graebe (*Annalen*, 1905, **340**, 251) gives m. p. 123—124°. The m. p. now recorded was obtained with specimens of ester prepared from the pure acid, m. p. 172—174°, synthesised from phthalic anhydride either by treatment with naphthalene in the presence of aluminium chloride (Graebe, *loc. cit.*) or with 1-naphthylmagnesium bromide (Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1937, **59**, 1028). The methyl ester, prepared by the action of diazomethane on *o*-1-naphthoylbenzoic acid, had m. p. 119—120°, in agreement with Graebe.

4-*Keto*-1-(1′-*naphthyl*)-3 : 4-*dihydrophthalazine* (4·4 g.) was obtained by 6 hours' heating at 120° of a mixture of ethyl *o*-1-naphthoylbenzoate (5 g.), hydrazine hydrate (5 c.c.), and absolute alcohol (10 c.c.). Recrystallised from xylene and from acetic acid, it formed colourless crystals, m. p. 252—253° (Found: C, 79·5; H, 4·6. $C_{18}H_{12}ON_2$ requires C, 79·4; H, 4·45%).

o-1-*Naphthylmethylbenzhydrazide* (II; R = CO·NH·NH_2).—A solution of 1-benzylnaphthalene-2′-carboxylic acid (10 g.) in absolute alcohol (300 c.c.) and sulphuric acid (8 c.c.) was refluxed for 5 hours. The colourless oil obtained was treated with hydrazine hydrate (10 c.c.)

and absolute alcohol (10 c.c.) and heated at 120° for 10 hours. The *hydrazide* formed colourless silky needles (8·0 g.), m. p. 175—176° (Found: C, 78·0; H, 5·85. $C_{18}H_{16}ON_2$ requires C, 78·2; H, 5·8%).

ω-1-*Naphthyl*-o-*tolylurethane* was obtained by gradual addition of sodium nitrite (2·2 g.) in water (10 c.c.) to a stirred solution of the above hydrazide (3·6 g.) in acetic acid (100 c.c.) and concentrated hydrochloric acid (10 c.c.) at 10°. After 1 hour, the solution was diluted with water (100 c.c.). The thick oil obtained was collected, dissolved in warm alcohol, and boiled for ¾ hour. The *urethane* formed colourless needles from alcohol, m. p. 113—114° (Found: C, 78·5; H, 6·2. $C_{20}H_{19}O_2N$ requires C, 78·65; H, 6·25%).

Hydrolysis of the urethane (0·5 g.) with concentrated aqueous ammonia (10 c.c.) in a sealed tube at 180° for 2 hours gave 1-o-*aminobenzylnaphthalene* (II, R = NH_2) in colourless needles, from alcohol, m. p. 101—102° (Found: C, 87·4; H, 6·25. $C_{17}H_{15}N$ requires C, 87·5; H, 6·4%).

My thanks are due to Professor J. W. Cook, F.R.S., for his interest in this work, to the Finney-Howell Research Foundation for a fellowship, and to the British Empire Cancer Campaign for a grant to this Institute.—The Chester Beatty Research Institute, The Royal Cancer Hospital (Free), London, S.W. 3. [*Received, May 19th*, 1941.]

Action of Alkaline-earth Chlorides on Emulsions stabilised by Sodium Oleate. By A. H. Adams and A. R. Martin.

From experiments on the partial coagulation of a standard emulsion in sodium oleate solution by salts of bi- and higher-valent metals, Martin and Hermann (*Trans. Faraday Soc.*, 1941, **37**, 30) concluded that the extent to which the interfacial film of acid-soap is destroyed by the formation of sols of metal-soap in the organic liquid peptised by oleic acid from the film is an important factor in determining the volume of oil thrown out. They found that the coagulating powers of the alkaline-earth chlorides were in the order Ba>Sr>Ca, but gave no analyses supporting their conclusion in the case of these salts. We have therefore broken their standard benzene emulsion with quantities of the alkaline-earth chlorides equivalent to the sodium oleate present in exactly the manner described by them, and analysed the yellowish oil left after evaporation of the separated benzene, and also the suspension in the aqueous phase. The results, each the mean of two determinations, were as follows, r being the ratio of oleic acid molecules (including oleate expressed as oleic acid) to metal atoms:

	Oil from benzene.		Suspension in water.	
Reacting salt.	Wt. (g.).	r.	Wt. (g.).	r.
$CaCl_2$	4·00	2·17	0·84	1·38
$SrCl_2$	4·20	2·28	0·83	0·93
$BaCl_2$	4·34	2·65	0·66	0·43

The oil phase contains the greater part of the reaction product, in which the ratio of oleic acid to metal exceeds that for the normal oleate. Moreover, this excess follows the same order as the coagulating powers of the salts, Ba>Sr>Ca. The conclusion of Martin and Hermann is therefore true also for the alkaline-earth chlorides.—Sir John Cass Institute, Jewry St., Aldgate, London, E.C. 3. [*Received, May 5th*, 1941.]